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THE GLANDS OF THE MUCOUS MEMBRANE OF THE GOAT ABOMASUM

By K. J. HILL
Department of Physiology and Histology, The University of Liverpool

During the course of physiological investigations on gastric secretion in the goat, it became necessary to have more detailed knowledge of the distribution of the various glands and cell types than was available from the literature. A detailed histological examination was therefore made of the abomasum of the adult goat, and the following account deals with the three main types of gland found in the mucous membrane.

MATERIALS AND METHODS

Three adult goats were used for this study. In each case the abomasum was removed immediately after death, incised along the greater curvature and washed free of blood and food material with normal saline. After pinning out under slight tension it was placed in neutral 5 % formol saline for 48 hr. A narrow strip from the lesser curvature, extending from near the omaso-abomasal junction to the pylorus, was then taken and divided into one inch lengths. The ends of the pointers in Pl. 1, fig. 1 indicate the level at which the strip was taken. Paraffin sections were cut longitudinally at 6 μ and stained with haematoxylin and eosin and by Masson's Trichrome (Light Green) method.

Variation in the number of parietal cells in the glands along the lesser curvature was investigated by the following method. Three sections taken at random from each block were examined and ten glands spaced throughout each section were selected. Only glands extending through the complete thickness of the mucosa were chosen. In these glands the parietal cells were counted and an average figure per gland was taken from the three sections examined. This was done for six blocks and thus the parietal cell content of 180 glands was counted. The total number of parietal cells per gland was not, of course, obtained, as only sections through the glands were examined. Peptic cells were similarly counted. In addition, sections were taken from other regions of the abomasum and were found to be similar in structure to those taken from the lesser curvature.

OBSERVATIONS

Seen by the naked eye (Pl. 1, fig. 1) the abomasum is separated from the omasum by a prominent ridge running at right angles to the long axis of the stomach. The abomasum itself is clearly divided into two parts, a peptic part marked by large folds running parallel to the long axis of the stomach, and a pyloric part which is almost entirely smooth except for two or three longitudinal folds near the pylorus. The abomasum is separated from the duodenum by the pyloric sphincter.

Histologically the mucous membrane of the omasum shows, to within about 5 mm. of the abomasum, a modified type of stratified squamous epithelium which is heavily

keratinized. The remainder of the omasal epithelium is not keratinized and terminates abruptly on the small lip separating the omasum from the abomasum (Pl. 2, fig. 2).

The simple columnar surface epithelium of the abomasum commences abruptly at the omaso-abomasal junction and continues to the pylorus. Three main types of glands are present in the mucosa, each forming a distinct region with some gradation into the other types. It is convenient, therefore, to describe the abomasal mucosa as possessing three regions—cardiac, peptic, and pyloric.

The cardiac region

There is some variation in the extent of this region, but in all three specimens compound tubular mucous glands are present at the omaso-abomasal junction (Pl. 2, figs. 2, 3). In one abomasum (goat 1) they extend for about 10 mm. from the omaso-abomasal junction, but in the other two only a few mucous glands are present, occupying a distance of 1–3 mm. An occasional parietal cell is present in the mucous glands nearer the peptic gland region. The presence of mucin was confirmed by staining sections with Southgate's mucicarmine (Carleton & Leach, 1947).

The peptic region

This is the true gastric gland region and it extends for about 10–12 cm. from the cardiac region. Peptic and parietal cells are present in the glands, and the parietal cells tend to be more numerous in the middle third of the gland (Pl. 2, figs. 4, 5). Compared with the glands of the simple stomach there is a tendency for the individual glands to be separated by a greater amount of interglandular connective tissue.

After counting the peptic and parietal cells by the technique already described, graphs were constructed showing the distribution of these cells throughout this region (Text-figs. 1, 2). The text-figures show that both parietal and peptic cells are most numerous at about 1 in. from the cardiac region and that there is then a gradual fall towards the pyloric region.

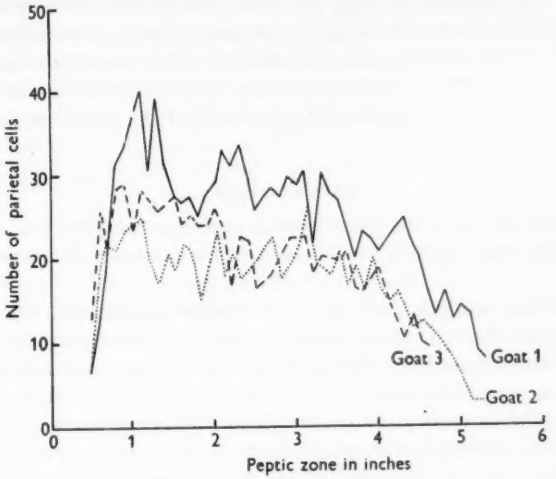
The pyloric region

This is of about the same length as the peptic region and it contains typical pyloric glands (Pl. 2, fig. 6). These terminate just beyond the pyloric sphincter at the commencement of the duodenal mucosa.

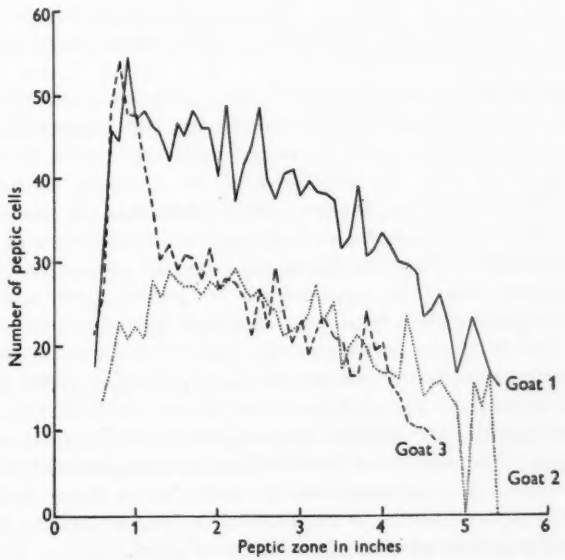
The abomasum from goat 1 shows an intermediate zone of approximately 1 cm. between the peptic and pyloric regions, consisting of mucous glands containing a few parietal cells. In the other two goats small islets of peptic glands are present in the pyloric gland region for a short distance after its commencement.

A characteristic feature of the whole of the abomasal mucosa is the presence of considerable accumulations of lymphoid tissue, extending, in some areas, from the muscularis to the surface epithelium.

Some sections were stained by the Bodian protargol method (Dawson & Barnett, 1944) to determine the distribution of argentaffine cells. These are numerous in the cardiac region and in the first 3–4 cm. of the peptic region. In the remainder of the



Text-fig. 1. Distribution of parietal cells in abomasal mucosa.



Text-fig. 2. Distribution of peptic cells in abomasal mucosa.

peptic region only a few scattered cells occur, but they are again numerous in the pyloric region. The argentaffine cells are found chiefly in the deeper regions of the mucosa and the individual cells occupy a peripheral position in the gastric glands.

Another constituent of the mucosa is a rounded cell containing a varying number of eosinophil granules. These cells are found between the columnar cells of the surface epithelium and in the glandular epithelium of the gastric glands.

DISCUSSION

The glandular nature of the abomasal mucous membrane and its division into peptic and pyloric regions has long been recognized, but the existence of a cardiac region has been disputed.

Some of the older workers could not find cardiac glands (see Oppel, 1896), and Haane (1905) states that the glands occurring at the omaso-abomasal junction were different in the three species he examined, resembling pyloric glands in the ox and cardiac glands in the sheep and goat. Bensley (1910) refutes this statement and considers that all these glands are cardiac glands, pointing out that Fröhlich (1907) had confirmed the existence of cardiac glands in all the domestic animals. Ellenberger (1911) describes the presence of true cardiac glands at the omaso-abomasal junction in the goat, and mentions the variation in width of the cardiac region and the presence of occasional parietal cells in the mucous glands. Both these observations have been confirmed in the present work. Lenkeit (1933), in his review of gastric secretion, states that there is no cardiac region in ruminants but gives no authority for his statement. Sisson & Crossman (1943) describe mucous glands, which they term cardiac glands, about the omaso-abomasal orifice of the cow and sheep.

This difference of opinion seems to have arisen partly because of the difficulty in deciding whether glands occurring at the omaso-abomasal orifice should be termed cardiac glands and partly because of the considerable variation in the extent of the region in different animals. The phylogeny of the ruminant stomach has been thoroughly investigated and, as Bensley (1902) points out, the complex stomachs such as those of ruminants, rodents, etc., are produced from the simple stomach by progressive specialization. The oesophagus takes no part in their development, the important phenomena being the suppression of the gastric glands and the replacement of the mucigenous epithelium by a stratified squamous epithelium. Oppel (1896) was the first to suggest that the cardiac glands formed an intermediate stage in the process of obliteration of the gastric glands. Bensley (1902) supports this suggestion and summarizes the evidence in its favour, concluding (p. 153) with a definition of cardiac glands as 'modified fundus glands occurring at the cardiac orifice of the stomach, or at the junction of the glandular and non-glandular divisions of the stomach, or in special sacs, differing from the usual fundus glands in the reduction in numbers, or complete absence of the parietal or ferment-forming chief cells, or both, and by the increased number of mucous chief cells'.

Accepting the definition that the cardiac glands are modified fundus glands occurring at the junction of the glandular and non-glandular divisions of the stomach, it seems justifiable to term 'cardiac' glands, the mucous glands described in this

paper as occurring at the omaso-abomasal junction, and the area of mucosa occupied by them, the 'cardiac' region.

The distribution of the peptic and parietal cells is of interest in that the maximum number of cells occurs a short distance from the cardiac region. The only other animal in which a comparable examination has been made is the cat, and Bowie (1940) has shown that in this species the peptic cells are few in number in the glands near the cardiac orifice, that they gradually increase to reach a maximum in the glands half-way along the fundus region and show a gradual fall towards the pyloric region.

The presence of an intermediate zone is a variable feature and this may account for the absence of any mention of such a zone in the goat by Billenkamp (1929), although he describes an intermediate zone in the calf abomasum.

Tehver (1930) describes argentaffine cells in the abomasum of the ox and sheep and states that they are almost entirely absent in the pyloric region of the sheep. According to Jacobson (1939), a similar distribution to that described in the present paper is seen in man and in the pig. Sharples (1945), however, using the Bodian technique, finds that argentaffine cells are relatively numerous all through the human stomach, and he attributes to inadequate impregnation the failure of previous workers to demonstrate them all. Although there may well be a species difference, the discrepancy between Tehver's results in the sheep and the present results in the goat may be explained by the greater selectivity of the Bodian method. Dawson (1944) has described the argentaffine cells in the rat as being periglandular, and Sharples (1945) has remarked on the considerable variation in shape of argentaffine cells in the human stomach.

The cells containing eosinophil granules appear to be identical with the cells found in the alimentary epithelium of the dog, cat and mouse and first described by Weill (1919) as 'Schollenleukozyten'. Keasbey (1923) later described similar cells in the abomasum of the sheep and termed them 'Globule leucocytes'.

SUMMARY

1. The abomasal mucosa from three goats has been examined histologically.
2. Cardiac, peptic and pyloric regions are described.
3. Considerable variation occurs in the number of peptic and parietal cells in the gastric glands.
4. The abomasum from one goat shows an intermediate zone between the peptic and pyloric regions.
5. The distribution of argentaffine cells in the abomasum is described.

My thanks are due to Prof. R. A. Gregory and Dr N. M. Hancox for helpful advice during the preparation of this paper and to Miss E. Price for technical assistance. I am indebted to Mr R. Harrison of this Department for preparing the microphotographs.

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EXPLANATION OF PLATES

Plate 1

Fig. 1. Goat 2. Abomasum opened along greater curvature.

Plate 2

Fig. 2. Goat 1. Omaso-abomasal junction. Haematoxylin-eosin; ×90.
Fig. 3. Goat 1. Cardiac mucous glands. Haematoxylin-mucicarmine; ×544.
Fig. 4. Goat 2. Peptic glands. Masson trichrome stain; ×115.
Fig. 5. Goat 2. Peptic glands. Masson trichrome stain; ×735.
Fig. 6. Goat 2. Pyloric glands. Masson trichrome stain; ×115.

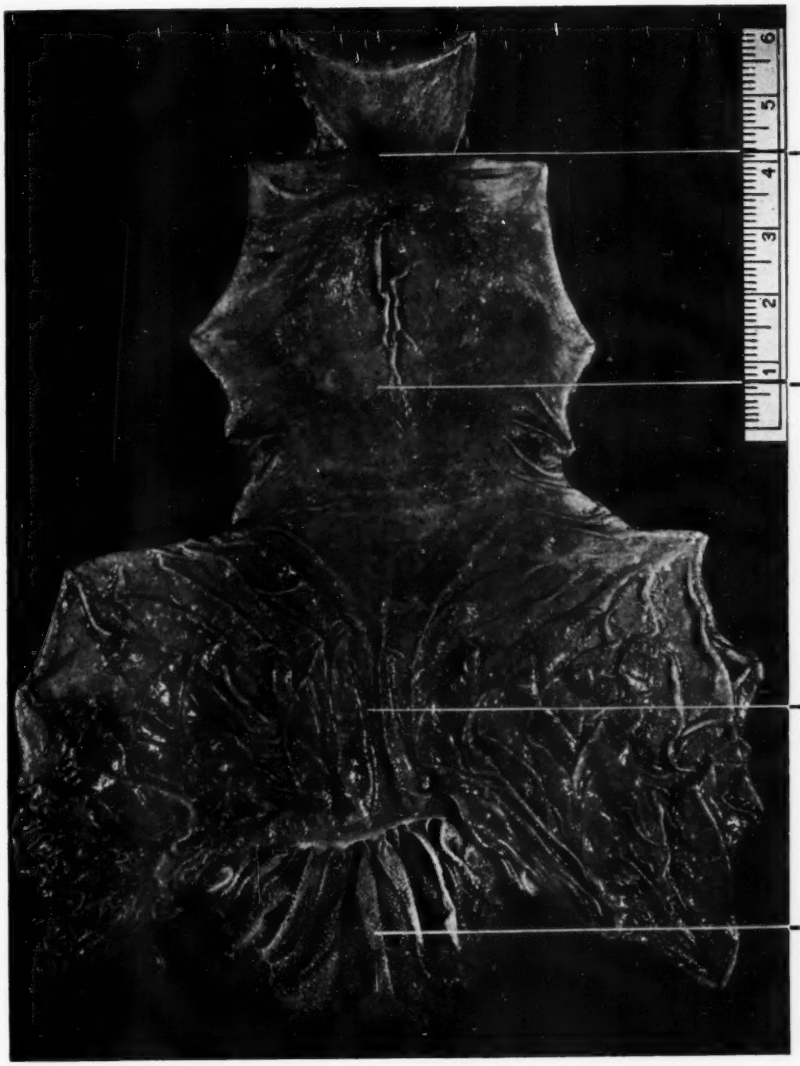


Fig. 1.

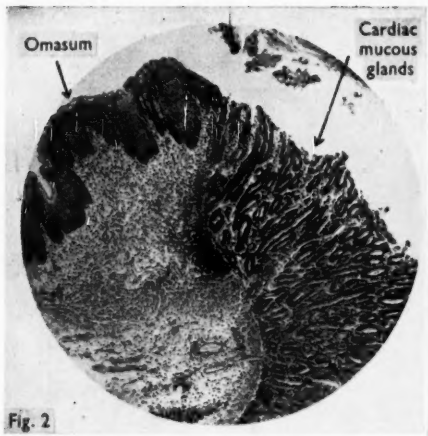
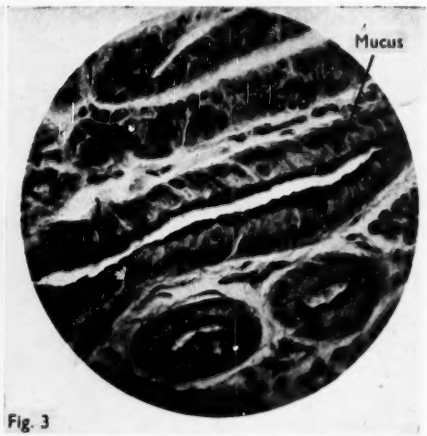


Fig. 2



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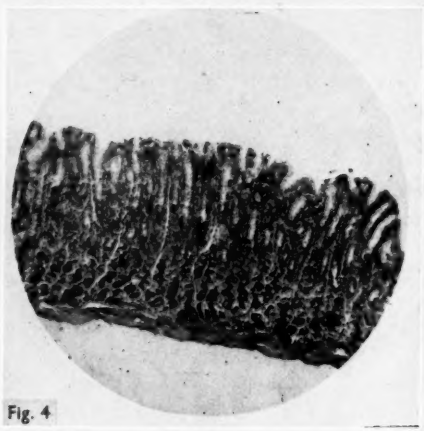
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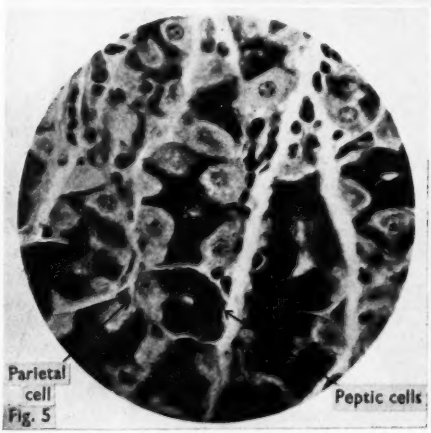


Fig. 5

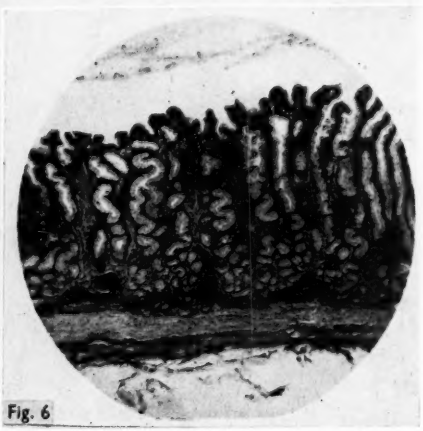


Fig. 6

HILL—THE GLANDS IN THE MUCOUS MEMBRANE OF THE GOAT ABOMASUM

FURTHER STUDIES OF THE METACARPO-PHALANGEAL AND INTERPHALANGEAL JOINTS OF THE THUMB

By J. JOSEPH, *Department of Anatomy, Guy's Hospital Medical School*

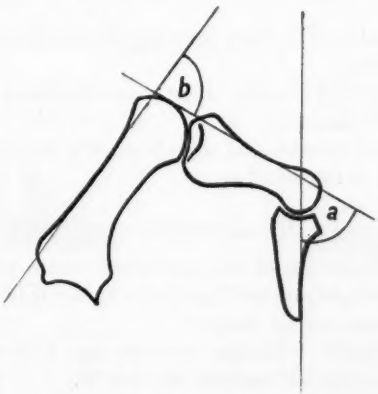
INTRODUCTION

In a previous paper (Harris & Joseph, 1949) it was observed that the metacarpo-phalangeal joint surfaces of the thumb varied considerably in shape; the majority had a rounded head on the metacarpal bone with a correspondingly concave base on the phalanx, but some thumbs showed a marked degree of flattening of both joint surfaces. Similar examples are shown in Pl. 1, figs. 1, 2. It was also observed that the latter type of joint was associated in some cases with limitation of flexion (Pl. 1, figs. 3, 4). It was decided that a detailed investigation of these 'flat' joints should be undertaken.

In the course of this study, a considerable number of thumbs were radiographed in the position of full flexion of the thumb joints, so that the variation in this movement at the metacarpo-phalangeal and interphalangeal joints was also investigated.

MATERIALS AND METHODS

The students and staff of the Department of Anatomy, University College, London, were the main source of the sample of ninety males and fifty-four females. Lateral views of their thumbs were taken with the metacarpo-phalangeal and interphalangeal joints fully flexed. The same axes for the metacarpal bones and phalanges were used as in the previous investigation, and the angles between the axes were measured to the nearest half degree (Text-fig. 1).



Text-fig. 1. Method used for measuring the interphalangeal and metacarpo-phalangeal angles. Angle $a = 60°$, angle $b = 83°$.

In addition, eleven subjects known to have 'flat' metacarpo-phalangeal joints and twelve known to have one or both metacarpo-phalangeal joints capable of an extension angle of over 40° were radiographed.

One hundred and fifty-nine dry first-metacarpal bones were examined and grouped according to whether the head was 'round' or 'flat'. Since it was suspected that the radiographic appearance of the shape of the head of the first metacarpal bone might be due to its position when photographed, sixteen first metacarpals with differently shaped heads were photographed in different positions.

As it was thought that there might be an hereditary basis for the differences in the joint surfaces, twenty-five sibs and some other close relatives of a series of subjects with 'flat' metacarpal heads had lateral views taken with their thumbs fully extended and flexed.

RESULTS

(1) *Interphalangeal joints*

Text-fig. 2 shows histograms of the maximum flexion angles of the interphalangeal joints of the right and left thumbs in ninety males and fifty-four females. The following conclusions can be drawn:

(*a*) There is considerable variation between one individual and another; the greatest angle observed was 92° and the smallest 24°.

(*b*) The distribution is fairly symmetrical. The means and standard deviations of the flexion angles of the right and left sides, in both sexes, are given in Table 1.

Table 1. *Means and standard deviations of flexion angles at the interphalangeal thumb joints*

Sex	Side	Mean	Standard deviation	Number of observations
Male	Right	65·37	10·58	90
	Left	65·03	12·98	90
Female	Right	67·44	11·74	54
	Left	66·35	10·80	54

(*c*) In both males and females there is no significant difference between the means of the right and left sides.

(*d*) In both right and left thumbs there is no significant difference between the means of the males and females.

(*e*) In both males and females, the angle is usually similar on both sides ($r = 0{\cdot}61$ in the males, and 0·59 in the females).

(2) *Metacarpo-phalangeal joints*

Text-fig. 3 shows histograms of the maximum flexion angles of the metacarpo-phalangeal joints of the right and left thumbs in ninety males and fifty-four females. The following conclusions can be drawn:

(*a*) There is considerable variation between one individual and another; the greatest angle observed was 88° and the smallest 5°.

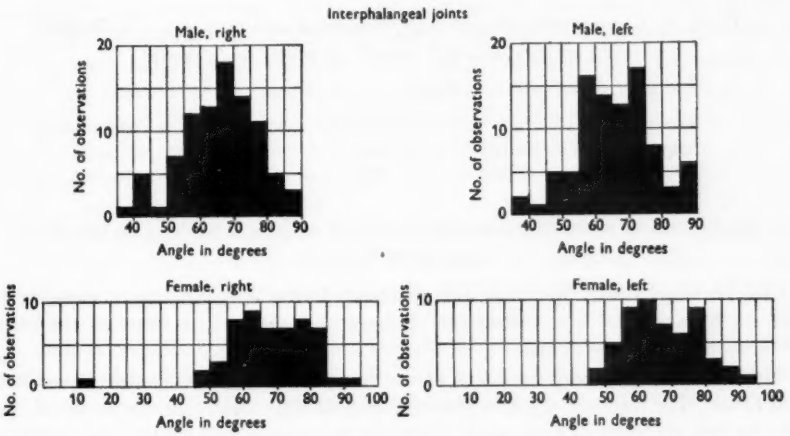
(*b*) The distribution is fairly symmetrical; the means and standard deviations of the flexion angles for the right and left sides in both sexes are given in Table 2.

(*c*) In both males and females there is no significant difference between the means of the right and left sides.

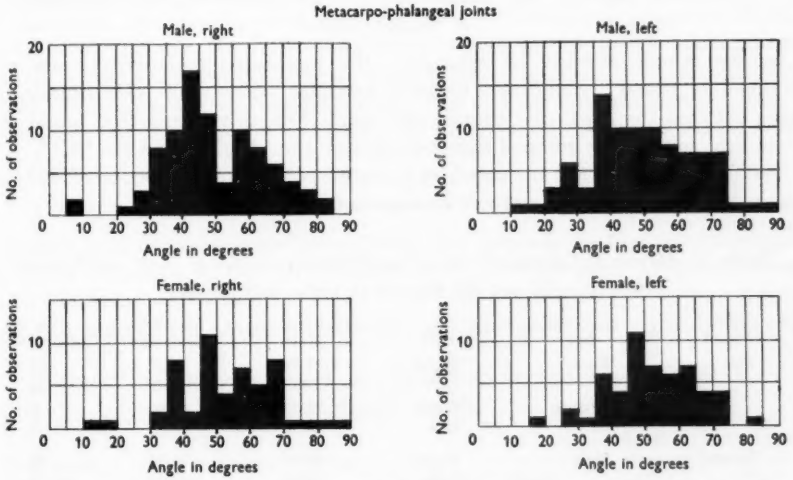
(*d*) In both right and left thumbs there is no significant difference between the means of the males and females.

Table 2. *Means and standard deviations of flexion angles at the metacarpo-phalangeal thumb joints*

Sex	Side	Mean	Standard deviation	No. of observations
Male	Right	52·56	14·68	90
	Left	52·07	13·07	90
Female	Right	48·40	15·71	54
	Left	49·21	15·51	54



Text-fig. 2. Histograms of angles of maximum flexion at the interphalangeal joints of the right and left thumbs in males and females.



Text-fig. 3. Histograms of angles of maximum flexion at the metacarpo-phalangeal joints of the right and left thumbs in males and females.

(*e*) In both males and females, the angle is usually similar on both sides ($r = 0{\cdot}79$ in the males and 0·78 in the females).

(3) *The interphalangeal compared with the metacarpo-phalangeal joints*

Maximum flexion at the interphalangeal joints may be related to maximum flexion at the metacarpo-phalangeal joints. The correlations between the two joints in the right and left thumbs of males and females were calculated (see Table 3), and it was found that there was no such correlation.

Table 3. *Correlations between interphalangeal and metacarpo-phalangeal joints of right and left thumbs in males and females*

	Males		Females	
Side	*r*	Observations	*r*	Observations
Right	+0·10	90	+0·21	54
Left	−0·12	90	+0·07	54

(4) *Flexion of metacarpo-phalangeal joint of subjects capable of an extension angle of 40° or more*

In a previous study, Harris & Joseph (1949) found that a group of subjects was able to hyperextend the metacarpo-phalangeal joint 40° or more if the carpo-metacarpal joint were flexed.

The mean and standard deviation of the flexion angles of these subjects are 52·87° and 11·35°. The number of joints observed was 32. The mean and standard deviation for the 288 metacarpo-phalangeal joints of the sample are 50·12° and 15·00° respectively. There is no significant difference between these two groups.

(5) *Flexion angles of 'flat' metacarpo-phalangeal joints compared with those of 'round' joints*

In the sample studied for extension, the metacarpo-phalangeal joints were classified as 'round', 'roundish', 'flattish', and 'flat', since there were intermediate types between the markedly 'round' and 'flat'. For convenience the 'round' and 'roundish' joints were grouped together, as were the 'flattish' and the 'flat'.

Table 4 gives the means and standard deviations of the angle of flexion of 'flat' and 'round' joints of the right and left thumbs in males and females.

Table 4. *Means and standard deviations of flexion angles of 'flat' and 'round' joints of right and left thumbs in males and females*

Type of joint	Sex	Side	Mean	Standard deviation	No. of observations
'Flat'	Male	Right	31·79	9·02	21
		Left	29·87	9·79	19
	Female	Right	33·33	10·60	6
		Left	33·94	10·85	7
'Round'	Male	Right	50·83	14·80	75
		Left	52·57	15·14	75
	Female	Right	54·30	12·43	50
		Left	54·70	10·86	50

The differences between the flexion angles of 'flat' and 'round' joints in both thumbs in males and females are highly significant and amount to 19·04° in the right and 22·70° in the left thumbs in males, and 20·97° in the right and 20·76° in the left thumbs of females.

(6) *Classification of dry first metacarpal bones according to the shape of the head*

One hundred and fifty-nine dry first metacarpal bones were examined and grouped according to whether the head was 'round' or 'flat' (Pl. 1, figs. 5, 6). There were one hundred and twenty-one 'round' and thirty-eight 'flat' heads, that is about 24 % of the total had 'flat' heads. This percentage should be compared with the fifty-five 'flat' metacarpal heads out of a total of 566 metacarpal bones examined in the study of extension of the thumb joint (Harris & Joseph, 1949), that is about 10 %. There is a marked difference between these two figures and it may be accounted for partly by the fact that the dry bones were mostly bones of old people, and the metacarpal head frequently showed signs of osteo-arthritis which tended to give a flattened appearance to the head.

It was also considered probable that the position of the bone, while being photographed, might influence the appearance of the shape of the head. Sixteen dry first metacarpals with differently shaped heads were radiographed in the following positions:

(1) True lateral, that is, no rotation of the shaft and the base and head in the same plane as the X-ray film.
(2) Head elevated, without rotation of the shaft.
(3) Base elevated, without rotation of the shaft.
(4) Medial rotation of the shaft, with the base and head in the same plane.
(5) Lateral rotation of the shaft, with the base and head in the same plane.

Of the ten bones classified as 'round', none appeared to be other than round in all five positions. Of the six bones classified as 'flat', all, except one, appeared round in one or more of the five positions, but never in all of them (Pl. 1, fig. 7). It is suggested that the incidence of 'flat' metacarpal heads is higher than the 10 % obtained from lateral radiographs of thet humb, because a certain number are missed owing to positioning, but that it is not as high as the 24 % obtained on examination of the dry bones.

(7) *Investigation of sibs of subjects with 'flat' metacarpo-phalangeal joints*

Table 5 gives the incidence of 'round' and 'flat' joints in the thumbs of males and females in the sample studied for extension. There is a significant difference between males and females ($\chi^2 = 10{\cdot}38$).

In this sample, thirty-one subjects (twenty-three male and eight female) had

Table 5. *Incidence of 'round' and 'flat' metacarpo-phalangeal joints in males and females*

Metacarpal head	Male			Female		
	Right	Left	Total	Right	Left	Total
'Round'	111	112	223	93	95	188
'Flat'	22	21	43	7	5	12

'flat' joints in one or both thumbs, and one or more sibs of thirteen of these had their thumbs radiographed in full flexion and extension. The total number of sibs examined was twenty-five. Of the twenty-six metacarpo-phalangeal joints of the thirteen male sibs, ten were 'flat', and among the twenty-four metacarpo-phalangeal joints of the twelve female sibs two 'flat' joints were found. There is no significant difference between this incidence and that of the sample.

DISCUSSION

The amount of flexion of the interphalangeal joint varies considerably in different people. Harris & Joseph (1949) discussed the possible causes for this in relation to extension, and one can only conclude that of the factors responsible (shape of joint surfaces, tendons, capsule, and ligaments), it is chiefly the tightness of the capsule which determines the amount of flexion movement at this joint, a conclusion similar to the one drawn when discussing extension. Since the means and standard deviations of the total range of movement at the interphalangeal joints, both in males and females, in both thumbs were regarded as useful they were estimated. The total range of movement is about 90° and the standard deviation about 13°. No significant difference is found between the two sides and between the sexes.

Movements at the metacarpo-phalangeal joint are complicated by the fact that different types of joints can be described, as was shown in the investigation into extension of the thumb joints. The range of variation of movement is more marked at this joint than at the interphalangeal joint. These differences between individuals are due either to the shape of the joint surfaces or to the capsule or both. A factor other than the joint surface must sometimes be responsible, since although it is shown quite conclusively that 'flat' joints have limited flexion as compared with 'round' joints, some of the 'round' joints also show a marked limitation of movement. This is almost certainly due to capsular differences between joints. It has been suggested that frequent trauma to the thumb, such as occurs in playing rugby, might produce capsular thickening and subsequent contraction, but the history of each subject was carefully taken and there never was any suggestion that such repeated trauma was a cause of limited movement.

The group of subjects who can hyperextend their metacarpal joints 40° or more if they flex the thumb at the carpo-metacarpal joint, does not show any difference in its range of flexion from that of the sample. It was suggested that laxity of the capsule anteriorly was the main reason for this hyperextension. Apparently the posterior part of the capsule in these subjects does not possess this laxity and thus increased movement in flexion does not take place in this group.

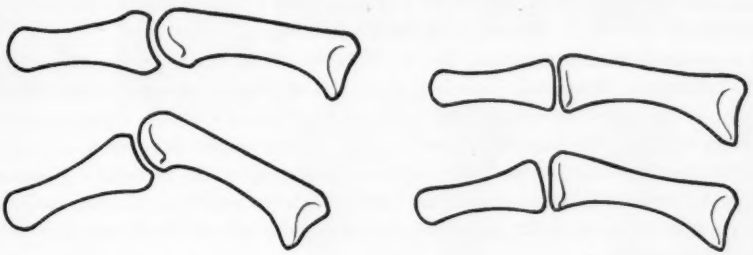
The most interesting group consists of those subjects who have what were described as 'flat' joints. It is fairly clear that labelling joints as 'flat' or 'round' by means of lateral radiographs is open to error in so far as some flat joints are missed due to the position in which the thumb is photographed. In addition, there are not two clearly defined types but a series of gradations from the commoner convex head to the relatively infrequent flat head.

From results obtained in this and other investigations certain conclusions can be drawn. The incidence is not less than 10 % found in the first sample studied and the condition is usually bilateral.

Those persons showing definite flattening have limited movement which is almost entirely confined to flexion, since the mean and standard deviation of the angles of extension of 'flat' joints were found to be similar to those of the whole sample. Subjects with 'flat' joints never hyperextend the metacarpo-phalangeal joint on flexing the metacarpal bone.

Consideration of the mechanical factors involved in movements at a so-called hinge joint explains why 'flat' joints have limited movement. The rounded head usually found on the first metacarpal allows not only bending but also gliding of the phalanx on the metacarpal. If the head is 'flat' the joint becomes a true hinge joint and gliding is reduced. The extent of movement achieved then depends largely on the opening up of the joint on its anterior and posterior aspects, which is equivalent to saying that it depends on the stretching of the capsule in front and behind (Text-fig. 4). This will also explain why hyperextension of 'flat' joints never occurs.

Examination of about 250 lateral radiographs of boys and girls aged 11 to 17 shows that 'flat' joints are present at an early age (Pl. 1, fig. 8).



Text-fig. 4. Outline of first metacarpal and proximal phalanx of the thumb, showing the effect of shape of joint on extent of movement. (*a*) Round joint: gliding and hinge movement. (*b*) Flat joint: hinge movement only.

To what extent is this condition familial? The figures presented for the sibs of subjects with 'flat' joints indicate that 'flat' first metacarpal heads do not occur in families to a significant extent. Wilgress (1898) described stiffness of the metacarpo-phalangeal joints of the thumb in a family in which two male cousins had bilateral stiffness of the joints; one of them had seven children of whom two males and two females showed this condition, and the other had one male child with a similar stiffness. In the present series, there were a father and three sons who all showed a marked limitation of flexion associated with 'flat' metacarpo-phalangeal joints in both thumbs. One of the sons said that he found it impossible to perform the Scout salute, that is, bringing the thumb far enough across the palm to allow its anterior surface to touch the nail of the little finger.

A striking feature of this condition of limited movement is the fact that only one other subject complained that this limitation caused some disability, and it may be added that there were seventeen thumbs each with a total range of movement of less than 30°. This should be compared with the means and standard deviations of the total range of movement at the metacarpo-phalangeal joints in both thumbs of both sexes in Table 6.

Table 6. *Means and standard deviations of total range of movement of metacarpo-phalangeal joints of both thumbs in males and females*

Sex	Side	Mean	Standard deviation	No. of observations
Male	Right	54·44	17·18	90
	Left	59·83	19·18	90
Female	Right	56·30	15·81	54
	Left	61·58	14·69	54

An attempt was made to see whether one could forecast the shape of the meta carpo-phalangeal joint by clinical examination of the amount of flexion found at the joint. Sixty male students were examined and thirteen were chosen as they appeared to have limited flexion. The incidence of 'flat' joints among these thirteen was nine out of twenty-six. This incidence, when compared with that of the first sampie, is just significantly greater ($\chi^2 = 4{\cdot}32$). It is therefore suggested that if, following an injury to the thumb, a patient appears to have limited movement of the metacarpo-phalangeal joint, the joint should be radiographed to make sure that the limited movement is not due to the shape of the joint surfaces.

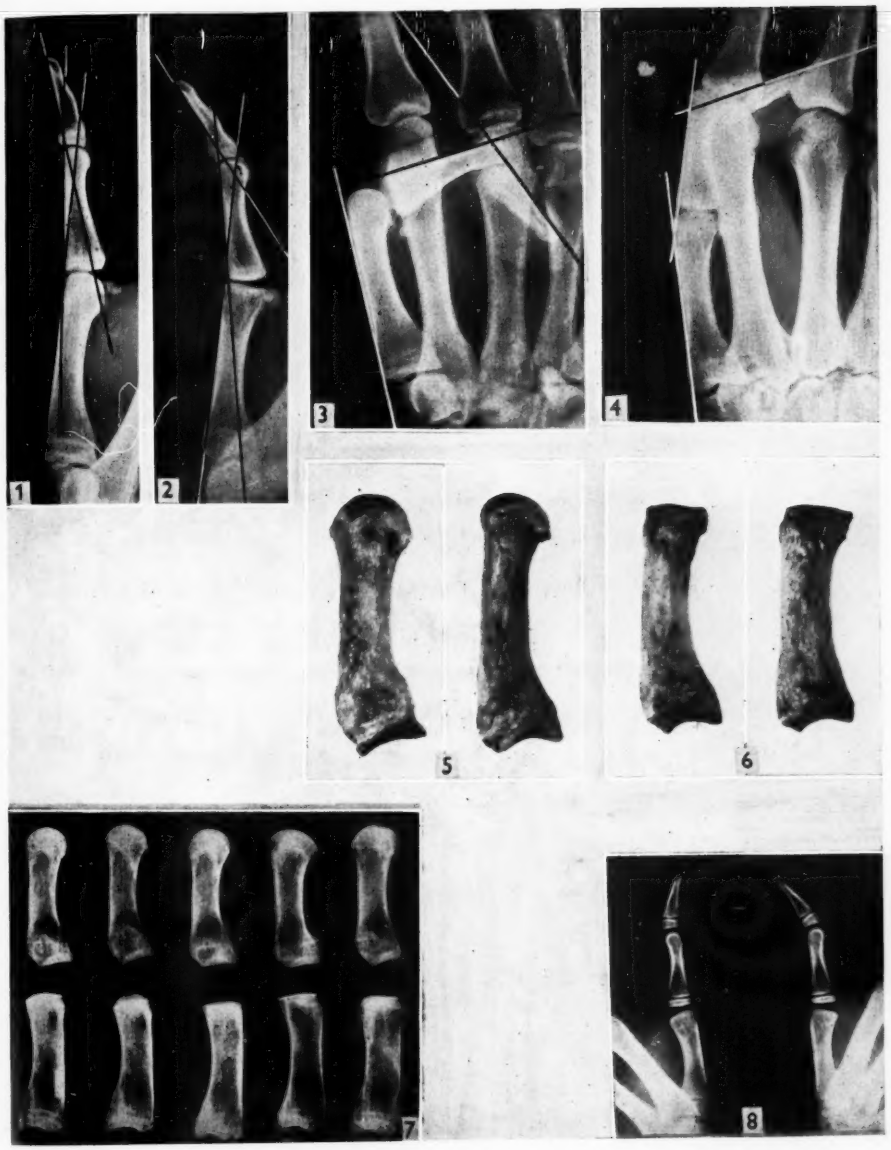
In a personal communication, Mr N. Roberts of the Orthopaedic Department, Royal Infirmary, Liverpool, commented on the apparently frequent association of stiffness in the metacarpo-phalangeal joint of the thumb with the clinical condition of hallux rigidus. He suggested that hallux rigidus might develop as a result of a limitation of movement due to a congenital flattening of the metatarso-phalangeal joint of the big toe. To what extent this latter condition occurs in the population and what its association with flat metacarpo-phalangeal joints of the thumb may be, are being investigated.

It was observed that many subjects, on maximally flexing the metacarpo-phalangeal and interphalangeal joints of the thumb, also flexed the terminal and sometimes the proximal interphalangeal joints of the index finger. If an attempt was made, either passively or actively, to straighten the index finger without decreasing the flexion of the thumb the subject complained of pain in the region of the front of the wrist or forearm on the lateral side. Straightening of the index finger could be achieved by reducing flexion of the thumb. If, however, the thumb was held passively flexed, the subject was able to straighten the index finger painlessly and completely. The explanation of this probably lies in the fact that, in these subjects, the flexor pollicis longus and that part of the flexor digitorum profundus going to the index finger are to some extent one muscle. From a study of the literature on the deep forearm muscles of the higher apes, this is perhaps not unexpected (Hepburn, 1892; Sonntag, 1942; Straus, 1942; Sullivan & Osgood, 1927), since in these animals flexor pollicis longus is either absent or small or part of flexor digitorum profundus.

SUMMARY

1. The range of variation in full flexion at the interphalangeal and metacarpo-phalangeal joints of ninety males and fifty-four females has been investigated.

2. There is considerable variation between individuals in maximum flexion at both joints of the right and left thumbs in both sexes.



JOSEPH—METACARPO-PHALANGEAL AND INTERPHALANGEAL JOINTS OF THE THUMB

3. The distribution for each joint in both thumbs in both sexes is fairly symmetrical, and there is a high correlation between the right and left thumbs for both joints in both sexes.

4. The maximum angle of flexion at the interphalangeal joint is not related to that of the metacarpo-phalangeal joint.

5. Subjects who, on flexing the carpo-metacarpal joint, can hyperextend their metacarpo-phalangeal joint, show no significant difference in flexion at this joint from the rest of the sample.

6. Subjects with 'flat' joint surfaces at the metacarpo-phalangeal joint show a significant decrease (about 20°) in flexion as compared with the rest of the sample.

7. 'Flat' metacarpo-phalangeal joints occur more frequently in males than in females, are usually bilateral and do not show hyperextension when the carpo-metacarpal joint is flexed.

8. The incidence of 'flat' joints determined by lateral radiographs of the metacarpo-phalangeal joint in full extension is about 10 %, but it is suggested that the incidence is greater since positioning may decrease the number found.

9. 'Flat' joints do not occur in families to a significant extent.

10. It is suggested that if metacarpo-phalangeal joints, when examined clinically, show limited movement, they should be radiographed in order to determine whether the limitation is due to a 'flat' joint, and that a similar flattening of the joint surfaces of the metatarso-phalangeal joint of the big toe may be related to hallux rigidus.

I wish to thank Prof. J. Whillis for reading and criticizing the manuscript; Dr H. Harris for assistance in statistics; the staff of the Department of Medical Illustration, Guy's Hospital; and all those people who so willingly submitted to having their thumbs radiographed, sometimes repeatedly.

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EXPLANATION OF PLATE

Figs. 1 and 2. 'Round' and 'flat' metacarpo-phalangeal joints.

Figs. 3 and 4. Flexion at 'round' and 'flat' metacarpo-phalangeal joints.

Figs. 5 and 6. First metacarpals with 'round' and 'flat' heads.

Fig. 7. Effect of different positions on appearance of head of first metacarpal (see text). Note the 'round' head in the second position of the 'flat' metacarpal.

Fig. 8. 'Flat' metacarpo-phalangeal joints in boy aged 12.

THE SESAMOID BONES OF THE HAND AND THE TIME OF FUSION OF THE EPIPHYSES OF THE THUMB

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INTRODUCTION

An investigation by Harris & Joseph (1949) into variations in the degree of extension at the joints of the thumb gave an opportunity of studying racial and sexual differences in the incidence of sesamoid bones in the hand. Since no accurate information regarding the time of appearance of these bones was available, radiographs of children's hands were studied, and this in turn led to an investigation of the time of fusion of the epiphyses of the thumb compared with those of the rest of the hand. Furthermore the relation between the extent of movement at the interphalangeal joint of the thumb and the presence or absence of a sesamoid has been studied.

Finally the relation of the interphalangeal sesamoid of the thumb to the tendon of flexor pollicis longus and to the capsule of the joint was investigated.

MATERIAL AND METHODS

Lateral radiographs of the right and left thumbs of 174 European males and 135 European females from 18 to 63 years of age, and of 31 male Indians and 30 male Africans were examined to determine whether sesamoid bones were present at the metacarpo-phalangeal and interphalangeal joints.

Of these radiographs, 135 European males, 124 European females, 17 Indians and 20 Africans were suitable for determining the incidence of sesamoid bones at the other metacarpo-phalangeal joints.

In addition, lateral radiographs of the right and left thumbs of 130 boys, aged 13–18 years, and of 102 girls, aged 11–16 years, were studied, and of these 124 males and 100 females were suitable for studying the sesamoids at the metacarpo-phalangeal joint of the index finger, and 46 males and 88 females for studying those of the little finger.

The degree of movement at the interphalangeal joint of the thumb was determined by the method discussed by Harris & Joseph (1949) and by Joseph (1951).

Finally the thumbs of 47 cadavers were dissected in order to study the relation of the sesamoid bone to the flexor pollicis longus and to the capsule of the interphalangeal joint of the thumb.

OBSERVATIONS

(1) *Interphalangeal sesamoid of the thumb*

(*a*) *Adults.* Table 1 shows the incidence of this sesamoid in male and female Europeans, and male Indians and Africans. All these subjects were regarded as 'adult' since the epiphyses of the hand were fused. The incidence of bilateral sesamoids in European males is 69 % and in European females 79 %, and this difference is barely significant.

Table 1. *Incidence of interphalangeal sesamoid of thumb in adults*

Subjects	Right and left present	Only right present	Only left present	Right and left absent	Total	Percentage with bilateral sesamoids
Male Europeans	120	5	7	42	174	68·98
Female Europeans	107	3	1	24	135	79·27
Male Indians	22	1	0	8	31	70·97
Male Africans	25	0	1	4	30	83·33

There is no significant difference between European and Indian and African males.

(*b*) *Children.* Tables 2 and 3 show the incidence of the interphalangeal sesamoid of the thumb in boys aged 13–18 years and girls aged 11–16 years.

Table 2. *Incidence of interphalangeal sesamoid of thumb in boys*

Age	Right and left present	Only right present	Only left present	Right and left absent	Total
13–14	2	0	0	18	20
14–15	2	2	0	13	17
15–16	15	3	0	18	36
16–17	21	0	0	12	33
17–18	19	0	0	5	24

Table 3. *Incidence of interphalangeal sesamoid of thumb in girls*

Age	Right and Left present	Only right present	Only left present	Right and left absent	Total
11–12	1	0	3	11	15
12–13	3	1	1	14	19
13–14	11	1	0	11	23
14–15	22	2	1	6	31
15–16	12	0	1	1	14

It can be concluded that in males the interphalangeal sesamoid appears between the ages of 13 and 18 years, but that the adult incidence does not occur until the age group 17–18 years is reached. On the other hand, it appears in females between the ages of 11 and 15 years and the adult incidence is reached by the age of 15 years. This variation in ossification time between individuals and the difference in sexes is in no way unusual.

(*c*) *Cadavers.* The thumbs of the cadavers showed that the tendon of flexor pollicis longus was easily separated from the front of the capsule of the interphalangeal joint, and that the sesamoid, when present, was embedded in the front of the capsule. Ten showed no evidence of this bone, but in these cases there was a definite thickening of the capsule where one would expect to find the bone. The size of the bone when measured varied considerably, ranging from a small ossicle about 1 mm. wide, 1 mm. long and 1 mm. thick to one as large as 4 mm. wide, 3 mm. long and 3 mm. thick. It was also possible to estimate the size of the bone in radiographs and in these it varied from a scarcely detectable speck to a bone 3 mm. thick and 3 mm. long. However, it was impossible to measure the width of the bone from the lateral view.

The dissected sesamoid always showed a small oval facet at its distal end and this facet articulated with the anterior part of the proximal surface of the distal phalanx.

(*d*) *Relation to movement.* Table 4 shows the relation between extension and flexion at the interphalangeal joint and the presence or absence of a sesamoid bone.

Table 4. *Means and standard deviations of angles of extension and flexion at the interphalangeal joint of the thumb with and without a sesamoid bone*

		With sesamoid			Without sesamoid		
Movement	Sex	Mean	Standard deviation	No. of observations	Mean	Standard deviation	No. of observations
Extension	Male	31·80	11·40	187	28·14	12·05	79
	Female	24·17	11·34	161	23·90	7·05	39
Flexion	Male	65·38	11·61	172	66·13	11·46	84
	Female	67·54	10·89	114	67·38	7·91	34

The range of movement at the interphalangeal joint shows no significant difference between those joints with a sesamoid bone and those without.

(2) *Metacarpo-phalangeal sesamoids*

Two sesamoids were seen at the thumb metacarpo-phalangeal joints in all adults, whether European, Indian or African.

Tables 5 and 6 show the incidence of these bones and of the interphalangeal sesamoid in the thumbs of boys and girls at different ages. It can be seen that the metacarpo-phalangeal sesamoids always appear before the interphalangeal and that they appear earlier in girls than in boys, varying considerably with regard to when they appear in any individual. It can also be concluded that the interphalangeal sesamoid never appears before the metacarpo-phalangeal sesamoids in the thumb. The above tables also suggest that these sesamoids mostly appear between 12 and 15 years in males and between 10 and 12 years in females. Flory (1936), Todd (1937), Francis (1940) and Flecker (1942) give similar ages for the time of their appearance.

Table 5. *Incidence of metacarpo-phalangeal (m.p.) and interphalangeal (i.p.) sesamoids of the thumb (boys)*

Age	No m.p., no i.p.	1 m.p. R. or L., no i.p.	2 m.p. R. and L., no i.p.	2 m.p. R. and L., 1 i.p. R. or L.	2 m.p. R. and L., 1 i.p. R. and L.	Total
13–14	12	1	5	0	2	20
14–15	3	3	8	2	2	18
15–16	1	1	16	3	15	36
16–17	1	0	11	0	21	33
17–18	0	0	5	0	19	24

Table 6. *Incidence of metacarpo-phalangeal and interphalangeal sesamoids of the thumb (girls)*

Age	No m.p., no i.p.	1 m.p. R. or L., no i.p.	2 m.p. R. and L., no i.p.	2 m.p. R. and L., 1 i.p. R. or L.	2 m.p. R. and L., 1 i.p. R. and L.	Total
11–12	5	1	7	1	1	15
12–13	1	2	11	2	3	19
13–14	0	1	10	1	11	23
14–15	0	0	6	3	22	31
15–16	0	0	1	1	12	14

Regarding the sesamoid bones at the other metacarpo-phalangeal joints, it was found that almost all the 135 male and 124 female adults could be arranged in three larger and two smaller groups (Fig. 1):

(*a*) Those with none.

(*b*) Those with bilateral ulnar sesamoids at the 5th metacarpo-phalangeal joint.

(*c*) Those with bilateral radial sesamoids at the 2nd and bilateral ulnar sesamoids at the 5th metacarpo-phalangeal joints.

(*d*) Those with a unilateral radial sesamoid at the 2nd or a unilateral ulnar sesamoid at the 5th metacarpo-phalangeal joint.

(*e*) Those with bilateral ulnar sesamoids at the 5th and a unilateral radial sesamoid at the 2nd metacarpo-phalangeal joint.

Table 7 gives the incidence of these groups in adult male and female Europeans and adult male Indians and Africans. The remaining 14 male and 16 female Europeans showed different combinations of sesamoids, and these are shown in Fig. 2. One African had 8 right and 7 left sesamoids, that is of the possible 16 sesamoids only the left 3rd metacarpo-phalangeal was missing.

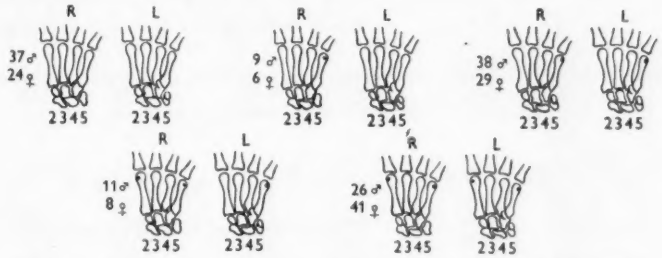

Fig. 1. Incidence of common arrangements of metacarpo-phalangea sesamoids in 121 male and 108 female European adults.

Table 7. *Incidence of metacarpo-phalangeal sesamoids in adult male and female Europeans and adult male Indians and Africans*

Subjects	None	One m.p. 2, or m.p. 5	Bilateral m.p. 5	Bilateral m.p. 5, unilateral m.p. 2	Bilateral m.p. 5, bilateral m.p. 2	Total
Male Europeans	37	9	38	11	26	121
Female Europeans	24	6	29	8	41	108
Indians	6	0	6	1	4	17
Africans	5	0	5	0	10	20

Tables 8 and 9 show the incidence of sesamoid bones at the 2nd and 5th metacarpo-phalangeal joints in male and female children respectively.

Table 8. *Incidence of sesamoids at 2nd and 5th metacarpo-phalangeal joints in male children*

		Age				
Joint	Sesamoid	13–14	14–15	15–16	16–17	17–18
M.p. 2	None	17	16	26	17	14
	Unilateral	1	0	1	6	1
	Bilateral	2	1	8	7	7
M.p. 5	None	13	12	6	3	None
	Unilateral	1	0	1	0	None
	Bilateral	1	1	6	2	None

Table 9. *Incidence of sesamoids at 2nd and 5th metacarpo-phalangeal joints in female children*

Joint	Sesamoid	Age 11–12	12–13	13–14	14–15	15–16
M.p. 2	None	15	15	18	17	7
	Unilateral	0	2	1	2	0
	Bilateral	0	2	3	11	7
M.p. 5	None	15	7	10	4	2
	Unilateral	0	1	3	4	2
	Bilateral	0	9	8	14	9

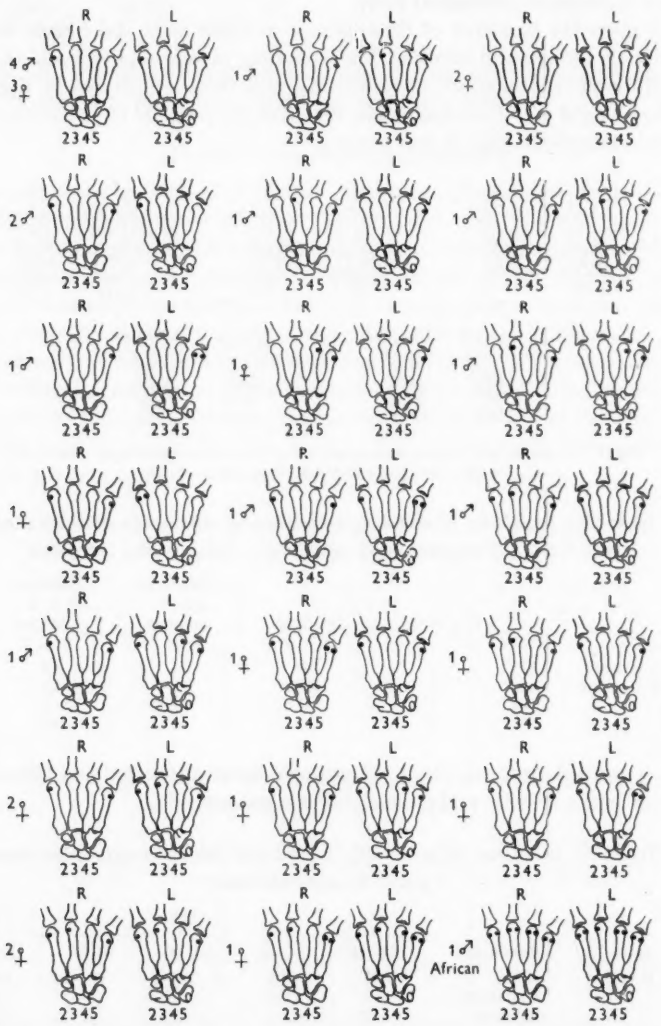

Fig. 2. Incidence of uncommon arrangements of metacarpo-phalangeal sesamoids in 121 male and 108 female European adults. (A very unusual arrangement in a male African is included.)

It can be concluded from the above tables that these sesamoids occur frequently only at the 2nd and 5th metacarpo-phalangeal joints in both males and females. Actually the incidence of the 5th is 70 % and of the 2nd 35 %. Furthermore, they appear at 15–18 years in males and 12–15 years in females. In the cases seen there is some evidence that in females the 5th appears before the 2nd. There is no evidence that there is any difference in the incidence of sesamoids between adult male Europeans and adult male Indians and Africans.

(3) *Fusion of thumb epiphyses*

The state of the epiphyses of the hand was classified under the headings of 'not fused' (where there was a complete gap between the epiphysis and the shaft of the bone), 'fusing' (where there was partial closure of the gap) and 'fused' (where there was complete closure of the gap). Tables 10 and 11 show the incidence of the number of fused epiphyses in male and female children.

Table 10. *Incidence of the number of fused epiphyses in male children*

(The most significant figures are shown in heavy type.)

State of epiphyses	Age 13–14	14–15	15–16	16–17	17–18
None fused	20	17	26	3	1
Thumb distal phalanx fused or fusing; rest not fused	0	0	**2**	**0**	**0**
Thumb metacarpal and distal phalanx fused; rest not fused	0	0	**4**	**7**	**1**
Thumb metacarpal and phalanges fused; rest not fused	0	0	**1**	**3**	**2**
All fused except metacarpals 2 to 5	0	0	1	5	0
All fused	0	0	2	12	18
Total	20	17	36	30	22

Table 11. *Incidence of the number of fused epiphyses in female children*

(The most significant figures are shown in heavy type.)

State of epiphyses	Age 11–12	12–13	13–14	14–15	15–16
None fused	15	15	14	1	0
Thumb distal phalanx fused or fusing; rest not fused	0	**2**	**3**	**1**	**0**
Thumb metacarpal and distal phalanx fused; rest not fused	0	**0**	**2**	**7**	**2**
Thumb metacarpal and phalanges fused; rest not fused	0	**0**	**2**	**5**	**3**
All fused except metacarpals 2 to 5	0	0	1	4	3
All fused	0	0	0	12	6
Total	15	17	22	30	14

It can be concluded that in males the epiphyses of the hand begin to fuse at the age of about 16 years and in females at about 14 years, and that the first to fuse is that of the terminal phalanx of the thumb. The next is the metacarpal of the thumb and following that, the proximal phalanx of the same digit; that is the thumb epiphyses fuse before all the others.

It has long been recognized that the first metacarpal may have an epiphysis at its distal end as well as the invariable one at its proximal end. Similarly the other metacarpals, although more rarely, may show an epiphysis or some evidence of an epiphysis at their proximal ends.

Flecker (1942) quoted Borovansky & Hnévkorsky, who gave a figure of 50 % for the incidence of a distal epiphysis on the 1st metacarpal and '70 % if grooves or fissures were included'. These percentages were found in an investigation of Prague boys. The appearance of an epiphysis at the proximal end of the 2nd metacarpal has been regarded as a rarity, though Thomson (1869), Freund (1905), Michaelis (1905) and Wakeley (1924) have each described one case, and Pryor has reported its occurrence in each of 3 children in 2 families (1906) and in each hand of quadruplets (1939).

Among the male children in the present series, 11 out of 20 in group 13–14 years showed evidence of distal epiphyses of the right and left 1st metacarpal and two showed this epiphysis on the right only. In the 14–15 group, three had right and left 1st metacarpal distal epiphyses and in the 15–16 group two had this epiphysis on the right and left and one on the right only. There was also one subject in the 16–17 group who showed this epiphysis on the right and left. Two boys in the 13–14 group had bilateral proximal epiphyses on the 2nd metacarpals.

In the female groups 11–12, 12–13, 13–14, and 14–15, one or two in each group showed evidence of distal 1st metacarpal epiphyses on each side.

It is suggested that a distal epiphysis occurs on the 1st metacarpal fairly frequently, and that it fuses earlier than the proximal epiphysis. The incidence in the male group 13–14 is striking. Allowing for a 2 years' difference between males and females, it is not surprising that the female groups show a small incidence. It would be instructive to radiograph girls younger than 11 years and boys younger than 13 years.

DISCUSSION

(1) *Sesamoids of the hand*

The incidence of bilateral interphalangeal sesamoids of the thumb is about 74 %. This is very similar to the 73 % incidence found by Pfitzner (1892) and also by Fawcett (1896) in his small series. The incidence of 22 % quoted by Bizarro (1921) is misleading and can almost certainly be explained by an examination of his age groups—54 out of 112 subjects were between the ages of 15 and 25 years. The younger members of that group, especially among males, would not have developed this bone.

It is important to note that occasionally the interphalangeal sesamoid occurs in only one thumb, since it is usually taught in clinical medicine that an accessory ossicle which may simulate a fracture is bilateral.

Pfitzner (1892) found the 5th metacarpo-phalangeal sesamoid in 75 % of the 388 hands which he dissected and the 2nd in 44 %. In the present series, the 5th was found in 70 % and the 2nd in 35 %. These differences may be due to the fact that Pfitzner dissected the sesamoids. Some of them may be missed if radiological methods of investigation are used. Furthermore, his subjects were much older than those in this series, and in the younger subjects some of the sesamoids may not yet have developed.

What causes the appearance of sesamoid bones and what their function is have

been questions which have engaged the attention of many investigators. Gillette (1872) maintained that sesamoids occur where pressure occurs and that they protect the tendons as they slide over articulations. He wrote at some length on the subject of the functions of the sesamoids and stated that age and muscular power determined their time of appearance and form. Retterer & Lelièvre (1911*a*, *b*) supported this theory by means of comparative anatomy stating that they found 'fibrous' sesamoids in the dog where tendons changed their direction, and where there was pressure and traction on and sliding of tendons. Retterer (1918*a–c*) maintained that sliding and rubbing modified the underlying cells and then pressure produced cartilage and bone. There have been many antagonists of this theory, and among them was Thilenius (1896) who showed that sesamoid bones were preceded by hyaline cartilage nodules before the muscles and joints were functioning. Pfitzner (1892) also maintained that they were not the result of pressure. Pearson & Davin (1920–1) supported him in his theory that sesamoids were vestiges of other bones but it is not clear what these other bones were. Bradley (1906) described the development of the sesamoid bones in the pig embryo and adult, and pointed out that all the toes have sesamoids, although only the 3rd and 4th digits are weight-bearing. His description of the sesamoid of the distal interphalangeal joint in the pig embryo is of considerable interest in view of the findings in the dissection of the human thumb interphalangeal sesamoid (see p. 231). He found that the sesamoid developed between the flexor tendon and the front of the joint, that it was at first attached to the distal phalanx and that a joint cavity subsequently developed between the two.

The present investigation has produced a considerable amount of evidence that sesamoid bones in the hand do not appear only in response to local environmental factors such as rubbing and pressure. First, they appear in males and females in approximately equal numbers. One would have expected a sex difference if pressure and muscular power were important factors. Secondly, they are almost invariably bilateral. They would have been more frequent in the right than in the left hand if the same factors were operating. Thirdly, the regularity of their time of appearance, that is between 13 and 18 years in males and 11 and 15 years in females and the manner in which they appear at an earlier date in females and at different times in different individuals indicate that ossification of the sesamoids is determined by factors similar to those which determine the ossification of any other bone in the body. Fourthly, it has been shown that the range of movement at the interphalangeal joint both in flexion and extension is not significantly different whether a sesamoid is present or absent. Consequently, angulation of the tendon round the joint is not a factor in determining the time of appearance of this sesamoid. In addition, the sesamoids of the thumb appeared in a fixed order, that is both the metacarpo-phalangeal sesamoids appear before the interphalangeal. This can be correlated with the fixed order of appearance of ossification centres and of the fusion of the epiphyses in each species (Stevenson, 1925). Thus it can be seen that the ossification of the sesamoids is similar to that of the rest of the skeleton in so far as:

(1) They ossify in a certain order.
(2) There are sex differences in their time of appearance.
(3) There are individual variations in their time of appearance.
(4) They are usually bilateral.

(5) Their appearance cannot be related to any known external environmental factors such as pressure or muscular power.

There is however one striking feature about the sesamoids as compared with the rest of the skeleton, namely the individual variation in their number, for although the majority of the subjects can be arranged in five groups there appears to be a large number of different groupings if the whole sample is considered. The occasional differences between the right and left hands are related to this. These variations can possibly be explained by the fact that, from an evolutionary point of view, these bones are disappearing.

It has also been observed that, as a rule, the little finger sesamoid is present if there is a sesamoid at the index finger and that both of these are present if there are sesamoids elsewhere.

As long ago as 1849, Pittard classified sesamoids into 'intratendinous' and 'periarticular'. This still influences some investigators to such an extent that the interphalangeal sesamoid of the thumb has been described as being in the tendon of flexor pollicis longus (Francis, 1940; Flecker, 1942). This was never found in the thumbs dissected in the present series. Similarly, the other sesamoids of the hand are embedded in the capsule of the joint and have an articular surface which articulates with the underlying bone. In the case of the thumb metacarpo-phalangeal sesamoids they are usually described as lying 'in the tendons of insertion of the flexor pollicis brevis and the adductor pollicis' (Cunningham, 1937), but it would be preferable to say that the tendons of the short thumb muscles are attached to the capsule of the joint where the sesamoids are embedded.

Flecker (1932) reported that both thumb metacarpo-phalangeal sesamoids were absent in a female aged 12 years and a male aged 15 years, and Bizarro (1921) reported two cases in whom these sesamoids were missing. The latter author does not give the age of his two subjects, but it is practically certain from his age distribution (54 subjects were between 15 and 25 years of age) that these sesamoids did not have time to develop. Consequently, it can be assumed that the thumb metacarpo-phalangeal sesamoids, as was found in the present series, are present in all adults.

(2) *Fusion of thumb epiphyses*

The present investigation indicates that the thumb epiphyses fuse before all the rest of the epiphyses in the hand, and that the thumb epiphyses themselves fuse in a different order from that of the other digits. In the thumb the order of fusion is distal phalanx, metacarpal, proximal phalanx. In the other digits it is distal phalanx, middle phalanx, proximal phalanx, metacarpal. This order of the fusion of the thumb epiphyses is found in both males and females and, as is usually the case, the females fuse 3–4 years earlier than the males.

A study of the literature shows that different authors noted one or more of these facts but not all of them. Sidhom & Derry (1930) pointed out that the epiphysis of the distal phalanx of the thumb was the earliest to fuse but did not suggest that the metacarpal united before the proximal phalanx nor did they differentiate between the sexes. Paterson (1930) baldly stated that all the phalanges and metacarpals unite in males at 19 years and in females at 17. Davis & Parsons (1927) suggested much later dates for the fusion of the epiphysis of the first metacarpal. Pryor (1933), to

whom must be given the greatest credit for emphasizing the sex differences in epiphysial fusion, gave the 'average' age of fusion of the epiphyses of all the metacarpals and phalanges as 19 years in males and 17 years in females. Shelton (1931) did not distinguish between the dates of fusion of the epiphyses of the thumb and the rest of the hand. Hellman (1928) stated that epiphysial fusion took place in the distal, then the middle, then the proximal phalanges, and finally in the metacarpal. Like Ruckensteiner (1931), he made no distinction between the thumb and the other digits. Todd (1933) stated that the order of fusion was distal phalanx, then proximal, then middle, although in his Tables he gave the same dates for the fusion of the proximal and the middle phalanges.

One can only speculate on the possible reasons for the earlier fusion of the thumb epiphyses as compared with the rest of the hand and the difference in the order of fusion. It may be related to the greater mobility of the thumb.

SUMMARY

1. The incidence of a bilateral interphalangeal sesamoid of the thumb is 74% in a sample population of 174 males and 135 females aged 18–63 years. This sesamoid appears in females between 11 and 15 years and in males between 13 and 18 years.

2. This sesamoid is in the capsule of the joint and not in the tendon of flexor pollicis longus. It always articulates with the anterior part of the proximal surface of the distal phalanx.

3. The range of flexion and extension at the interphalangeal joints which have a sesamoid is not significantly different from the range of movements in joints without a sesamoid.

4. The sesamoids at the metacarpo-phalangeal joint of the thumb are found in 100% of adults, and appear in females between 10 and 12 years and in males between 12 and 15 years.

5. The metacarpo-phalangeal sesamoids of the thumb always appear before the interphalangeal sesamoid.

6. There are three main groups of the other metacarpo-phalangeal sesamoids of the hand; (*a*) those with none, (*b*) those with bilateral 5th metacarpo-phalangeal sesamoids, (*c*) those with both bilateral 2nd and 5th metacarpo-phalangeal sesamoids. These sesamoids appear at 15–18 years in males and 12–15 years in females.

7. Investigation of a group of Indians and Africans does not suggest any racial differences in the incidence of the sesamoids of the hand.

8. The thumb epiphyses fuse earlier than, and in different order from, the epiphyses of the rest of the hand. The thumb epiphyses fuse as a rule between 15 and 17 years in males and 13–15 years in females.

9. A distal epiphysis of the metacarpal of the thumb occurs fairly frequently.

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THE FRAGILITY OF NON-MYELINATED NERVE TERMINALS

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It has been demonstrated (Weddell & Zander, 1950) that nerve fibres in freshly excised untreated corneas can be seen under the phase-contrast microscope. In a subsequent paper (Zander & Weddell, 1951) a description of the anatomy of corneal innervation has been given, in which this method was used to confirm and extend observations made following the use of a variety of other techniques. The method has definite limitations, however, for it cannot be used to examine the untreated living cornea *in situ*. Thus its value in the study of the morphology of nerve fibres in the cornea depends upon the rapidity with which the fibres undergo structural changes after severance of the connexion with their parent axons. It seemed advisable, therefore, to study the behaviour of corneal nerve fibres in excised corneas at intervals following their removal. We were further encouraged to carry out such observations in view of the work of Engelmann (1867) and Ranvier (1881), both of whom state that within a few hours after removal changes can be seen in the nerve fibres and corneal corpuscles of corneas kept in moist chambers. They give no details of the changes, but report that after a time the nerve fibres become beaded.

MATERIAL AND METHODS

Tangential sections were taken from the corneas of anaesthetized (intravenous nembutal) rabbits and monkeys, which were subsequently killed, and from the corneas of recently dead human subjects, and whole corneas were removed from rats and frogs. Immediately after they were obtained the specimens were placed on microscope slides in either anterior chamber fluid, 'physiological' saline, or saline containing 5 or 20 % commercial formalin (40 %), and covered with glass slips which were ringed with vaseline to prevent evaporation. In the case of the whole corneas, two radial incisions were made with sharp scissors before mounting so that they would lie flat on the slide. The specimens were then examined at intervals under the phase-contrast microscope. No attempt was made to control the temperature of the specimens during the course of the experiments.

OBSERVATIONS

The serial observations which follow refer mainly to the frog's cornea, in which the sequence of changes, although similar, evolves more slowly than in mammals, and is therefore easier to record.

(1) *Frog's cornea mounted in* 0·64 % *saline solution*

Immediately after mounting. It is only possible to distinguish the faint outline of non-myelinated nerve bundles in the substantia propria, close to their point of entry into the cornea and along the line of the radial incisions. The nerve fibres have an

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appearance which is commonly assumed to be 'normal'. Myelinated nerve fibres in the bundles at the limbus are clearly outlined. No isolated single nerve fibres can be seen, despite the fact that the fibrous texture of the substantia propria is quite distinct and the nuclei and boundaries of the epithelial cells are sharply demarcated. Very few corneal corpuscles can be seen, however, and no Schwann cells are visible (Pl. 1, fig. 1).

30 *min. after mounting.* Bundles of nerve fibres containing faint outlines of Schwann cells can now be clearly seen in the substantia propria. The contours of the axis cylinders are sharp and they appear 'normal', except that some of them contain small swellings along their course, which gives them a slightly beaded appearance. A few faintly outlined single axis cylinders can now be seen in the substantia propria, but no nerve fibres are yet visible in the epithelium. More corneal corpuscles can be seen and those previously seen faintly are now clearly outlined. Both nerve fibres and corneal corpuscles are seen most clearly in the periphery of the cornea and in relation to the radial incisions (Pl. 1, fig. 2).

40 *min. after mounting.* More nerve bundles and single nerve fibres can be seen in the substantia propria and the Schwann cells are more clearly outlined. Most of the axis cylinders are finely beaded; a few appear smooth in outline, and a few are coarsely beaded, having in addition small, highly refractile spheres lying beside them. No nerve fibres can be seen in the epithelium. More corneal corpuscles can be seen and their processes are now very clearly outlined. As before, the changes recorded are all most clearly seen around the periphery of the cornea and in relation to the radial incisions, but some nerve fibres can now be seen throughout the substantia propria of the cornea.

50 *min. after mounting.* Still more nerve fibres are visible in the substantia propria and more axis cylinders are coarsely beaded and have refractile spheres associated with them. The spheres present at the time of the previous examination are now larger. The majority of the axis cylinders are finely beaded, but some single nerve fibres in the substantia propria appear quite normal and smooth in outline. These fibres are seen to end in a series of beads. A few smooth and a few beaded nerve fibres can for the first time be seen in the basal layer of the epithelium.

60 *min. after mounting.* The substantia propria, particularly in the periphery of the cornea and in relation to the radial incisions, appears to contain as many nerve fibres as a completely stained or impregnated specimen, but the nerve fibres are not all 'normal' in appearance. Those ending in the substantia propria still appear 'normal'; the remainder have fine or large beads along their course and the number which have small highly refractile spheres beside them is increasing. Many more nerve fibres can now be seen in the epithelium: a few smooth in outline, the majority finely beaded, but a few with large beads along their course. An occasional highly refractile sphere can now be seen in relation to the coarsely beaded fibres.

70 *min. after mounting.* An increasing number of highly refractile spheres can be seen throughout the cornea; they are chiefly associated with nerve fibres in the substantia propria, but a few are associated with nerve fibres in the epithelium, and also with the processes of corneal corpuscles which can now be clearly distinguished in increasing numbers. Some of the refractile spheres associated with nerve fibres in the substantia propria close to the limbus now appear to replace the whole axon

instead of lying beside it. The number of nerve fibres seen in the epithelium in the centre of the cornea is relatively less than in a fully stained specimen. Throughout the period following the removal of the cornea the Schwann cells gradually become more clearly demarcated; a few, particularly in the periphery of the cornea and in relation to the radial incisions, now appear to contain beaded threads within their cytoplasm (Pl. 1, figs. 3, 4).

90 *min. after mounting.* The changes have progressed still further in the manner already outlined. There are now more nerve fibres visible in the epithelium.

145 *min. after mounting.* The majority of the axis cylinders in the substantia propria have refractile spheres along their course, the exception being those fibres which terminate in the substantia propria. In some cases the Schwann cells are so shrunken and distorted that, together with the nerve fibres associated with them, they appear to lie within channels in the substantia propria.

The number of nerve fibres in the epithelium is now comparable with that seen in a fully stained or impregnated specimen; a number of axons, however, are coarsely beaded and have refractile spheres in relation to them; the majority are finely beaded; a very few appear relatively smooth in outline (Pl. 1, figs. 5–7).

12 *hr. after mounting.* Myelinated axons in the substantia propria show signs of degenerative changes; the myelin is beginning to fragment and the axons are grossly distorted. Very few non-myelinated nerve fibres or recognizable Schwann cells can be seen in the substantia propria. In their original position are spaces which at first sight look like 'lymph' channels, but in fact they have no visible endothelial lining. A few coarsely beaded (in some cases fragmented) nerve fibres—those which terminate in the substantia propria—can still be seen. In the epithelium some coarsely beaded nerve fibres are still visible with refractile spheres along their course. Many nerve fibres have disappeared, leaving only refractile spheres to mark their original position. The corneal corpuscles are now very distinct, their processes being particularly clearly outlined. Some cells are visible in the substantia propria which are difficult to identify. They are smaller and have fewer processes than the corneal corpuscles, and their cytoplasm is almost clear.

24 *hr. after mounting.* The 'empty' channels have disappeared from the substantia propria and it is no longer possible to identify any nerve fibres except in the epithelium where a few large, highly refractile, spheres can still be seen lying along the course originally taken by nerve fibres.

(2) *Rat's cornea mounted in* 0·72 % *saline solution*

The sequence of changes in the corneal nerve fibres is similar to that seen in the frog save that the time taken to reach the final stages of disintegration is much shorter. For instance, there are a few nerve fibres clearly visible in the epithelium immediately after mounting, while 30 min. after mounting a large number of epithelial nerve fibres are seen, some of which are coarsely beaded and associated with refractile spheres. Twelve hours after mounting the appearances are similar to those seen in the frog's cornea 24 hr. after mounting.

(3) *Sections from monkey and rabbit cornea mounted in anterior chamber fluid or in* 0·72 % *saline solution*

The changes are similar to those seen in whole specimens from the rat except that they take place even more quickly, depending to some extent on the thickness of the sections. The most severe changes are seen in relation to the cut surface, or surfaces, of the section (Pl. 2, figs. 9–12). The changes were the same whether the specimen was in saline or fluid from the anterior chamber of the eye.

(4) *Sections from the human cornea* 4 *hr. following death* (Pl. 2, fig. 13)

The specimens, immediately after mounting, resembled those seen from the monkey about 120 min. after mounting.

(5) *Summary*

Very soon after the removal of the cornea, the nerve fibres, which at first are completely invisible, gradually become visible until they are sharply outlined. At first they are smooth, or only very finely beaded, in outline: appearing, in fact, morphologically 'normal'. As time goes on, the axons become more coarsely beaded until after 40 min., in the frog, refractile spheres are seen lying beside those in the substantia propria; later still the spheres come to lie along the course of the axon, seeming to replace the whole of a small segment of it. Lastly, the entire axon vanishes, its original position being occupied by a fluid-containing channel.

The nerve fibres most quickly affected are those closest to the point of their section, or closest to points of damage which may be assumed to have divided axis cylinders. The nerve fibres in the epithelium are affected last; they are farthest from the position of section. Since there is a gradual diminution in the diameter of nerve fibres from their point of entry into the cornea to their terminations (Zander & Weddell, 1951) it is also true to say that axons of larger diameter are more quickly involved than those of smaller diameter, but with one exception: nerve fibres ending in the substantia propria are more 'resistant' to these changes than any other corneal nerve fibres.

(6) *Frog's cornea mounted in* 5 % *formol-saline solution*

Immediately after mounting. The condition is almost exactly the same as that seen 60 min. after mounting in 0·64 % saline solution, except that the number of refractile spheres in the substantia propria is considerably less and no refractile spheres can be seen in association with the epithelial nerve fibres.

30 *min. after mounting.* In the substantia propria the number of nerve fibres associated with refractile spheres has increased; in particular, some axis cylinders appear to have split to enclose the spheres. The number of nerve fibres seen in the epithelium has increased, but very few have refractile spheres in relation to them although they are all, to some extent, beaded.

12 *hr. after mounting.* No refractile spheres can now be seen in association with the nerve fibres in the substantia propria. All nerve fibres have swellings along their course except those ending in the substantia propria, which remain smooth in outline. Some axis cylinders are distorted, having apparently split into two parts; others appear to pursue somewhat irregular courses. In the epithelium fewer nerve fibres

are seen; those which are visible are beaded and the course they pursue is more irregular than usual.

(7) *Frog's cornea mounted in* 20 % *formol-saline solution*

Immediately after mounting. Only a few fragmented single nerve fibres, having large refractile spheres associated with them, are seen in the substantia propria. Their terminations form an extensive network of apparently empty channels lying in a pattern similar to that occupied normally by nerve fibre bundles. No nerve fibres can be seen in the epithelium, but there are a number of refractile spheres in positions similar to those normally occupied by nerve fibres (Pl. 1, fig. 8).

12 *hr. after mounting.* The same distorted single nerve fibres are seen in the substantia propria. The apparently empty channels in the substantia propria have disappeared, and so have the refractile spheres in the epithelium. The whole structural organization of the cornea is grossly distorted.

(8) *Sections from mammalian corneas mounted in formol-saline solutions* (Pl. 2, fig. 14)

The changes were in no way different from those seen in the case of the frog.

In none of the specimens examined was it possible to see epineurial connective tissue sheaths surrounding nerve bundles in the cornea, nor was it possible to demonstrate the presence of endoneurial tubes.

The outline of the corneal epithelial cells is well seen under phase-contrast conditions, and so are the protoplasmic bridges passing between the cells in the deeper epithelial layers. Care has to be taken not to mistake cell outlines for nerve fibres, particularly since the protoplasmic bridges may be mistaken for beading. It is, however, only in the earliest stages that any doubt exists. Later, nerve fibres are easily recognized and can be traced in continuity for long distances, as can be seen in the photomicrographs.

DISCUSSION

On the one hand, our observations suggest that untreated corneal nerve fibres are *smooth* and either faintly visible or invisible under phase-contrast conditions. On the other hand, we have already shown (Weddell & Zander, 1950) that methylene-blue stained *beaded* nerve fibres in the human cornea are capable of conveying pain impulses when stimulated, and apparently suffer no irreversible change. In other words, the anatomy of non-myelinated corneal nerve fibres is labile, and it is probable that some beaded nerve terminals are as normal as non-beaded terminals, the morphological differences probably being due to physico-chemical activity of one kind or another in close relation to the axon. These observations imply that non-myelinated nerve terminals in the cornea are morphologically unstable. Indeed, they suggest that they have no 'static' anatomy such as that possessed by myelinated nerve fibres in a nerve trunk (Glees, 1943).

Our observations in this paper, and in a preceding one (Weddell & Zander, 1950) have shown that one of the chief factors contributing to the apparent morphological instability of non-myelinated terminals in the cornea is their extreme delicacy. Their behaviour suggests, indeed, that they consist solely of a fluid-containing boundary membrane unsupported by an endoneurial tube; and it may well be that changes in the permeability of the boundary membrane would lead to loss of fluid from the interior,

which in turn causes the axon to assume a beaded appearance. The series of morphological changes which the nerve fibres undergo *in vitro* after interruption of the connexions with their parent axons are essentially similar to those which occur in the course of degeneration *in vivo* (Zander & Weddell, 1951). In addition, a comparison of Pl. 2, figs. 9, 15 and 16, suggests that methylene-blue colours the axoplasm whilst silver is precipitated on the boundary membrane. There are differences in the order in which nerve fibres of different size are affected, but this may well be related to the fact that the severed ends of the axons are not sealed *in vitro* as they are *in vivo*.

The work of Young (1944*a*, *b*), Weiss (1943), Speidel (1932), and others, suggests that under normal conditions axons are maintained in a state of 'turgor' by influences emanating from the cell body to which the axon is attached; and Young (1944*a*) has suggested that the morphological changes in axons separated from their parent cells result from loss of this 'turgor'. Our observations are in keeping with these suggestions. In addition, we have shown (Zander & Weddell, 1951) that, following keratotomy, newly formed nerve fibres sprout from the normal non-myelinated terminals surrounding the lesion and advance towards the region of sensory loss. This observation suggests that there is sufficient 'turgor' or driving-force for nerve fibres to extend their terminals when not restrained from so doing by the presence of neighbouring nerve fibres (see Weiss, 1941). Moreover, the observations of Gutmann & Sanders (1943), that during regeneration the diameter of axons in the central stump decreases while that of the fibres developing from them increases, suggest that there is a pressure and movement of substance within nerve fibres. It seems not unreasonable, therefore, to suppose that non-myelinated nerve terminals, as the result of the wear and tear in everyday life, are continuously 'modifying' the tissue fluid spaces around them, at the expense of turgor pressure. This notion is possibly supported by the findings of Brücke, Hellauer & Umrath (1949), who state that following section of the ophthalmic division of the Vth cranial nerve in rabbits, precautions being taken to prevent keratitis, the acetylcholine content of the cornea increases slightly in the first few hours, then decreases rapidly, and at the end of the first day is up to 50 % less than that in the opposite, unoperated cornea.

So far no reference has been made to non-myelinated nerve terminals in situations other than in the cornea. This is due to the fact that, on technical grounds, the use of phase-contrast microscopy for the examination of nerve terminals in the manner we have employed for the cornea is not possible in other tissues. However, it is possible to compare the behaviour under normal conditions and during the course of degeneration of non-myelinated nerve terminals in the cornea, following methylene-blue staining and silver impregnation, with the behaviour of such terminals in other tissues; and the results are found to be very similar indeed (Weddell & Glees, 1941; Weddell, Guttmann & Gutmann, 1941; Weddell, Sinclair & Feindel, 1948; Zander & Weddell, 1951). Thus it seems reasonable to suppose that non-myelinated nerve terminals, in general, are morphologically unstable and it is even possible that they may have 'trophic' functions to perform in addition to the transport of action potentials.

Finally, the observations in this paper make it quite clear why there are so many contradictory statements in the literature concerning the anatomy of non-myelinated nerve terminals. The work of Boeke (1949), Reiser (1935–6, 1936–7) and Stöhr (1941),

particularly in relation to the sympathetic ground plexus, the periterminal network, and terminal reticulum, are clearly suspect in view of our observations on the effect of formalin fixation in relation to non-myelinated nerve terminals in the cornea. Stöhr, in particular, advocates the use of 50% formalin as a fixative, which is certainly responsible for the artefacts he describes.

SUMMARY AND CONCLUSIONS

1. Non-myelinated nerve terminals in the cornea undergo rapid degenerative changes when severed from their parent axons.

2. The form taken by the degenerative changes suggests that they result from a loss of 'turgor'.

3. The behaviour of non-myelinated corneal nerve terminals following separation from their parent axons suggests that they consist solely of a fluid-containing boundary membrane unsupported by an endoneurial tube.

4. There is evidence that non-myelinated nerve terminals in positions other than the cornea are morphologically similar.

5. It seems not unreasonable to suppose that non-myelinated nerve terminals, as the result of the wear and tear of everyday life, are continuously adding 'material' to the tissue fluid spaces around them under the influence of 'turgor' pressure.

6. The reaction of non-myelinated nerve terminals to formalin fixatives explains why there are so many contradictory statements in the literature concerning their morphology.

This investigation was made possible by a grant from the Rockefeller Foundation, to whom we wish to express our gratitude. We would also like to thank Mr Patrick Selwood and Miss Jean Gurden for their technical assistance.

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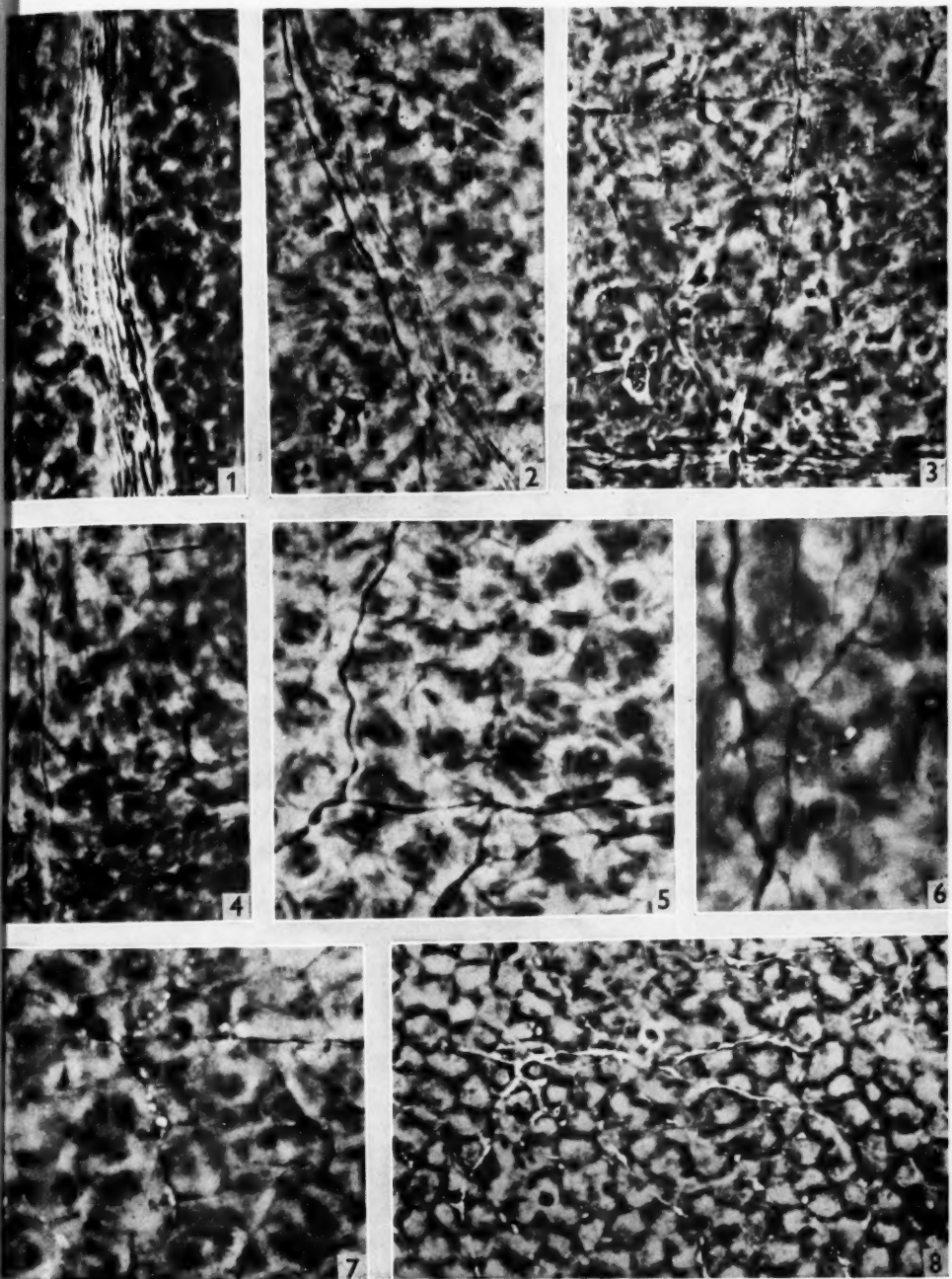
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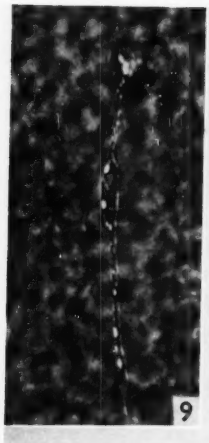
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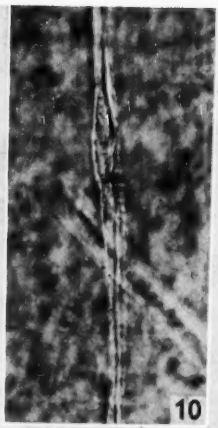
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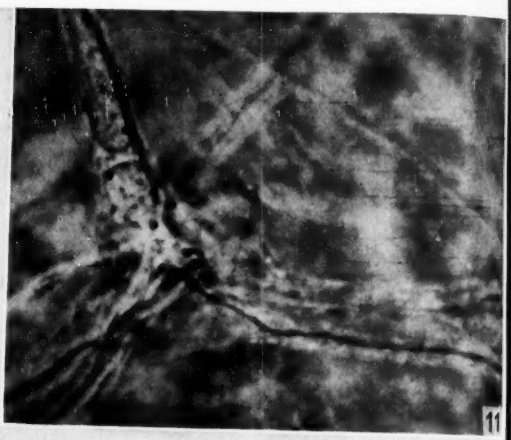
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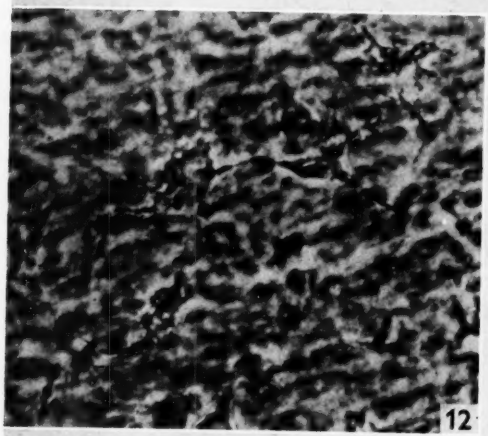
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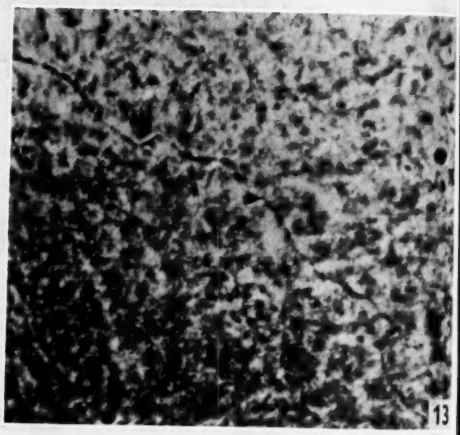
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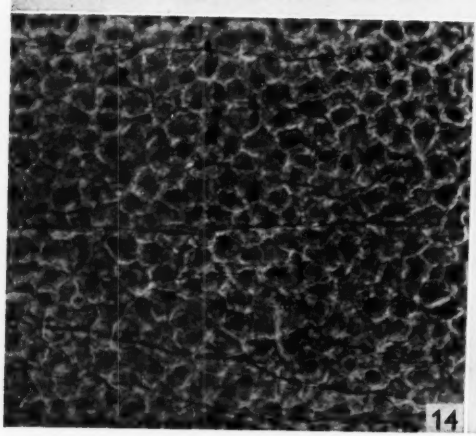
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EXPLANATION OF PLATES

PLATE 1

Figs. 1 to 7 are from a whole preparation of frog's cornea mounted in 0·64% saline solution under a cover-slip ringed with vaseline. The microscope used to obtain these photographs was a new Zeiss-Winkel standard model fitted with annular phase plates.

Fig. 1. This photograph was taken immediately after mounting and shows a nerve bundle close to the limbus containing myelinated and non-myelinated nerve fibres. The myelinated axons are sharply demarcated; the non-myelinated axons are only faintly outlined. (× 600.)

Fig. 2. This photograph was taken 35 min. after mounting. It shows a 'normal' nerve bundle in the substantia propria and a single nerve fibre which is somewhat swollen and beaded. (× 600.)

Fig. 3. This photograph was taken 70 min. after mounting. It shows a number of axons in the substantia propria, close to the limbus. Most of them are beaded: some finely, others more coarsely. Some axons have refractile spheres lying beside them. (× 600).

Fig. 4. This photograph was also taken 70 min. after mounting. It shows a finely beaded axon in the more superficial layer of the substantia propria near the centre of the cornea. (× 600.)

Fig. 5. This photograph was taken 145 min. after mounting. It shows many nerve fibres ramifying among the cells in the basal epithelial layer in the centre of the cornea. The axons are mostly beaded, but the beads are fine. (× 1000.)

Fig. 6. This photograph was taken 180 min. after mounting and shows nerve fibres ramifying among the more superficial epithelial cells towards the periphery of the cornea. Some axons appear almost 'normal' in part of their course; others are swollen and beaded, and some are represented only by refractile spheres. (× 1100.)

Fig. 7. This photograph was taken 300 min. after mounting. It shows fragmented axons lying among the epithelial cells. The axons have many refractile spheres associated with them. (× 1100.)

Fig. 8. This photograph was taken immediately after mounting a freshly excised cornea in 20% formol-saline. It shows a series of 'empty' channels in the position usually occupied by nerve fibres ramifying among the cells of the basal epithelial layer. (× 600.)

PLATE 2

Figs. 9 to 11 are from sections of rabbit cornea mounted in 0·74% saline solution under cover-slips ringed with vaseline.

Fig. 9. This photograph was taken from the periphery of the section 55 min. after mounting. It shows an axon associated with refractile spheres lying on a shrunken Schwann cell. (× 500.)

Fig. 10. This photograph was taken from the section 55 min. after mounting. It shows an apparently 'normal' axon lying on the surface of a Schwann cell which is itself very slightly shrunken. It appears to be surrounded by fluid. (× 500.)

Fig. 11. This photograph was taken from the centre of a section 90 min. after mounting. It shows Schwann cell pathways in the substantia propria. The Schwann cell nuclei are granular; the cytoplasm is slightly shrunken and covered with refractile spheres associated with disintegrating axons. One axon, apart from slight beading, appears almost 'normal'. This axon was seen to terminate in the substantia propria. (× 950.)

Fig. 12. This photograph was taken from a position close to the surface of a section from a monkey's cornea 90 min. after mounting. It shows the corneal corpuscles particularly clearly. Their cell bodies are shrunken, and their processes are beaded and associated with refractile spheres. (× 900.)

Fig. 13. This photograph is from a section of human cornea removed 4 hr. after death and mounted in Ringer's solution under a cover-slip ringed with vaseline. It was taken 15 min. after mounting. In particular it shows a coarsely beaded single axon in the substantia propria. (× 550.)

Fig. 14. This photograph is from a section of rabbit cornea mounted in 5% formol-saline. The photograph was taken immediately after mounting. It shows beaded nerve fibres ramifying among the epithelial cells. Some of the axons appear to have split into two in part of their course. (× 400.)

Fig. 15. This photograph is from a methylene-blue stained rabbit cornea. It shows a single degenerating axon lying beside a fine beaded normal axon in the substantia propria of a cornea in a region of partial sensory loss 5 days following keratotomy. The methylene-blue appears to colour the axoplasm more than the boundary membrane. (× 100.)

Fig. 16. This photograph is from a silver impregnated rabbit cornea. It shows a single degenerating axon in the substantia propria in a region of complete sensory loss 2 days following keratotomy. The silver appears to have precipitated on the boundary membrane of the axon. (× 900.)

THE EXTENSOR APPARATUS OF THE FINGER

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The study of the movements of the digits has attracted the attention of many workers (see Bunnell, 1942, 1944; Duensing, 1944; Braithwaite, Channell, Moore & Whillis, 1948, for the literature). But though agreement has been reached on many points there are others that are still poorly understood, particularly the peculiar interactions of the joints on each other.

LIMITATION OF FLEXION AT THE TERMINAL JOINT

When a finger is fully flexed on the palm (fig. 1A) the middle joint (proximal inter-phalangeal) is bent to an acute angle, while the distal joint (distal inter-phalangeal) is bent to about a right angle, with some variation in different individuals. From

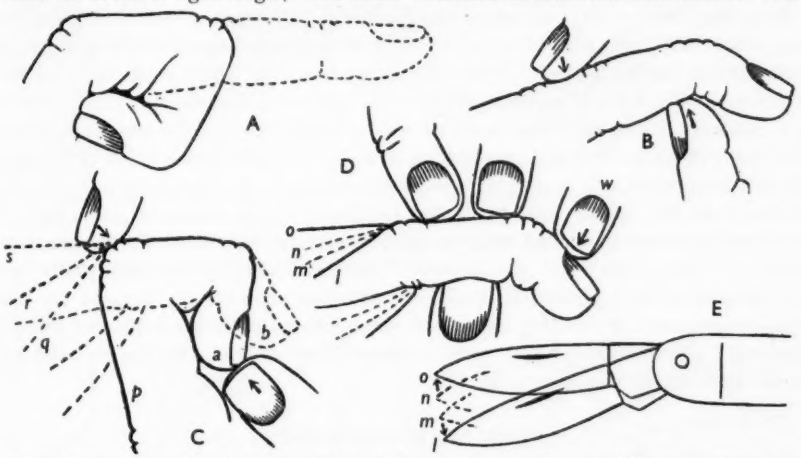

Fig. 1. Linked movement in the living subject. A, flexion and extension of middle finger; B, flexion of terminal joint with middle joint fixed in extension; C, effect of gradual extension of middle joint on flexion of terminal joint; D, production of snapping movement at middle joint; E, snapping in pocket-knife.

this position the finger can be extended completely. But when the middle joint is fixed in extension (fig. 1B), and an attempt is made, either by the subject or by the experimenter, to flex the terminal phalanx, it is found that it can, in most subjects, no longer be bent to a full right angle, but only through 45° or 60°.

Now if the middle phalanx be fixed in position while the distal joint is kept passively flexed by pressure between the finger and thumb (fig. 1C), the linked motion by which changes in the middle affect the distal joint can be studied in detail. As the middle joint extends from a position of full flexion, it has at first, position

p to *q*, no effect on the distal joint. As it passes through the middle part of its range, *q* to *r*, the distal joint extends from *a* to *b*, but the last part of the movement, *r* to *s*, has no effect.

A reciprocal movement of the middle joint when the distal joint is moved is difficult to demonstrate in the living subject. If, however, the middle phalanx is fixed, and at the same time pressure is maintained on the dorsum of the terminal phalanx by the finger (Fig.1D) a new phenomenon appears. Near the position of full extension, between *m* and *n*, the joint works smoothly, but on either side of this range a distinct springiness is felt, for the middle joint tends to spring suddenly into full extension, *n* to *o*, or into partial flexion, *m* to *l*. The sensation is similar to that felt on opening the blade of a pocket knife, for this again, beyond the neutral range, tends to spring into a fully open or a partially closed position. Thus the pressure on the terminal phalanx has induced a 'snappiness' in the middle joint, and made its motion similar to that of the well-known 'Schnappgelenke' found, for example, in the elbow of the horse and the knee of wading birds, fully discussed by Palmgren (1929, *a* and *b*) and Fick (1931), who bring together all previous work on the subject. In animals the snap-mechanism is often of biological significance, but in man it is only an epiphenomenon, induced by artificial conditions.

Schloffer (1909, p. 551) described the limitation of flexion at the distal joint, and suggested that it was due to an attachment of the dorsal aponeurosis through the joint capsule to the dorsum of the middle phalanx, but there is, in fact, no such attachment (Fig. 2A). Duensing (1944, p. 150) suggested that the limitation was due to a tautness in the side-slips (*s.sl.*) of the extensor aponeurosis when the middle joint was extended. But in a preparation in which the aponeurosis is cut (Fig. 2B, C) the link movement still takes place, and indeed in both directions, for not only does extension of the middle lead to partial extension of the terminal joint, but also flexion of the terminal joint induces some degree of flexion of the middle joint. Again, as Fick (1931) and many earlier workers have shown, snap-joints have peculiarities of their ligaments, which are attached eccentrically beyond the main axis of movement, so that they are at maximum tension at the labile phase ('kritische Stellung', 'punto morto'), and, once movement has started, tend to pull the joint in one direction or the other (Fig. 2F).

THE LINK LIGAMENTS

Dissection reveals two ligamentous bands, one on either side of the digit, passing from the sides of the distal part of the proximal phalanx, where some of the fibres are continuous with the proximal annular fibres of the fibrous flexor sheath, across the collateral ligaments of the middle joint, to join the extensor tendon on its way to the terminal phalanx (fig. 2A, *l.l.*). So long as these 'link' ligaments are intact the linked motion between the joints is found, but when they are cut it is lost. Forcible flexion of the terminal joint puts tension on the ligaments, which then tend to pull the proximal phalanx into partial flexion or full extension (Fig. 2D, E), with the characteristic springy motion.

The link ligaments have escaped the notice of most authors, but seem to be the structures shown as unlabelled slips by Seifert (1919, Abb. 1), who makes no comment on their significance. They are quite distinct from the thin fasciae which connect the

dorsal aponeurosis to the sides of the capsule of the middle joint figured by Bunnell (1942, fig. 5A).

LIMITATION OF EXTENSION IN THE TERMINAL JOINT

It is well known that when the middle joint is fully flexed the distal joint cannot be fully extended by active movement (fig. 3A), though it offers no resistance to passive extension (Fig. 3B). If now the middle phalanx is fixed (Fig. 3C) and the middle joint gradually extended, it is found that in the range w to x there is no change in the degree of active extension possible, from x to y the range gradually increases till the terminal joint can be fully extended, and from y to z there is no further change.

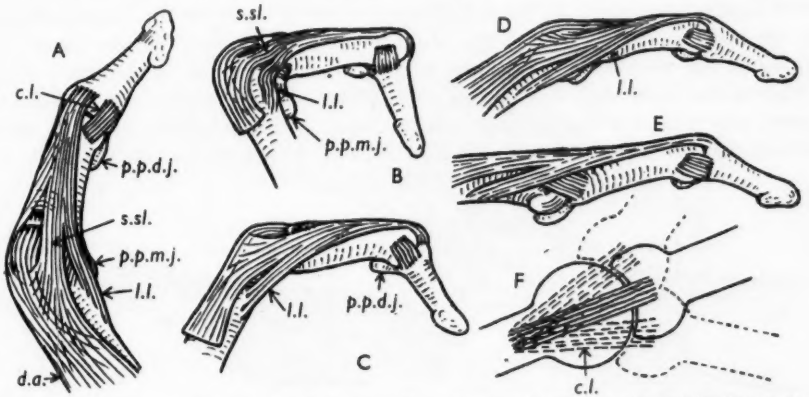

Fig. 2. Linked movement in an anatomical preparation. A, general dissection of a middle digit to show linked ligaments; B, link ligaments slack when middle joint is flexed; C, link ligaments tightened by extension of middle joint; D and E, movement of link ligament across axis of middle joint; F, snap mechanism after Fick (1931). For lettering see key on p. 259.

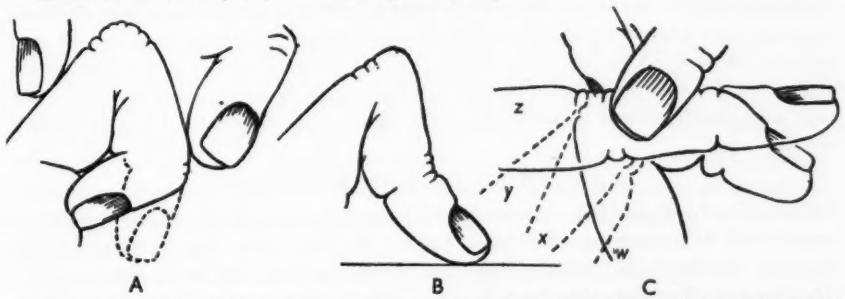

Fig. 3. Extension in distal joint. A, limits of active movements when middle joint is flexed; B, passive extension of terminal joint; C, effect of extension of middle joint.

This limitation is due to a slackness of the side-slips of the extensor aponeurosis when the middle joint is flexed, for in that position the side-slips lie on the volar side of the joint axis, and cannot be tensed by muscle action on the dorsal aponeurosis (Fig. 2B). As the middle joint nears its position of extension the side-slips pass more dorsally in relation to the joint (Fig. 2C), and transmit tension on the aponeurosis to

the terminal phalanx. The dorsovolar shift of the side-slips and its physiological effects are discussed fully by Schöning (1887), Bunnell (1942, 1944), Duensing (1944) and others, but still seem little known, so that the whole of the extensor system may be shown lying dorsal to the middle joint even when that joint is flexed (e.g. Braithwaite *et al.* 1948, fig. 2).

COMBINED EFFECTS OF THE LINK AND SHIFT MECHANISMS

Starting from a fully flexed position (Fig. 1A), the basal joint can be extended independently of the other two, but the middle and distal joints usually extend together. The relative amount of movement in the two joints can be controlled to some degree, presumably by the independent action of the flexor digitorum sublimis on the middle joint, but the degree of independence is limited. For in the earlier stages of the movement the tendon to the terminal phalanx is absolutely slack owing to the volar shift mechanism, and in the later stages the link mechanism comes into play and the terminal joint extends with the middle. Thus in most individuals there is little power of independent movement of the two joints.

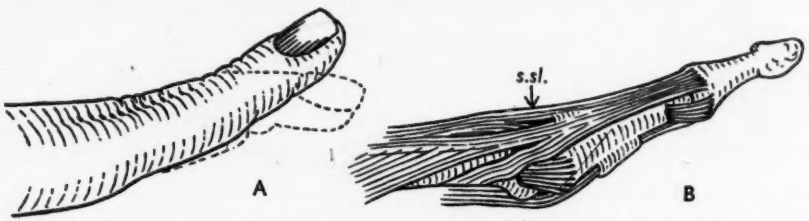

Fig. 4. Independent control of terminal joint. A, in living subject; B, anatomical mechanism. For lettering see key on p. 259.

Exceptional individuals who can move the terminal joint independently of the others can only do so after fixation of the middle joint in a position of hyperextension, by a constant tension on the dorsal aponeurosis, whose taut side-slips can be seen beneath the skin (Duensing, 1944, cf. my Fig. 4). Tension on the profundus tendon then gives flexion of the terminal joint without unlocking the middle joint. But most individuals cannot hyperextend the middle joint sufficiently for it to become locked.

LINK ACTION OF THE INTEROSSEI

A dissection of a finger (Fig. 5) shows that the general arrangement of the interosseous muscle with its tendon resembles that of a link ligament, and suggests that when the muscle is isometrically contracted its 'ligamentous action' will be similar to that of the ligament. The two structures have in common a proximal bony attachment, a volar relationship to a proximal joint, and a distal attachment to the dorsal aponeurosis. In fact, if in a fixed specimen with mobile joints and the interossei intact the proximal (metacarpo-phalangeal) joint is extended, the middle joint is vigorously extended at the same time. This linked action plays a part in the smooth stretching of the fingers, when the proximal and middle joints are extended at the same time. It is the counterpart of that described by Braithwaite *et al.* (1948), in which the common extensor contracts isometrically and the interossei actively.

ARRANGEMENT OF THE EXTENSOR ASSEMBLY

Some details of the anatomy of the extensor assembly, aptly so named by Bunnell (1942), may now be considered. Figs. 5–8 were prepared from a dissection of a single formalin-fixed right middle digit.

The two heads of the interosseous muscle combine in the intermetacarpal space but the common mass soon splits to form two distinct bellies, a superficial (*s.b.i.*) passing to the dorsal aponeurosis, and a deep (*d.b.i.*) passing to the base of the proximal phalanx, with some attachment to the palmar pad of the proximal joint. This is in agreement with Bunnell's dissection (1942, fig. 6D), but not with his

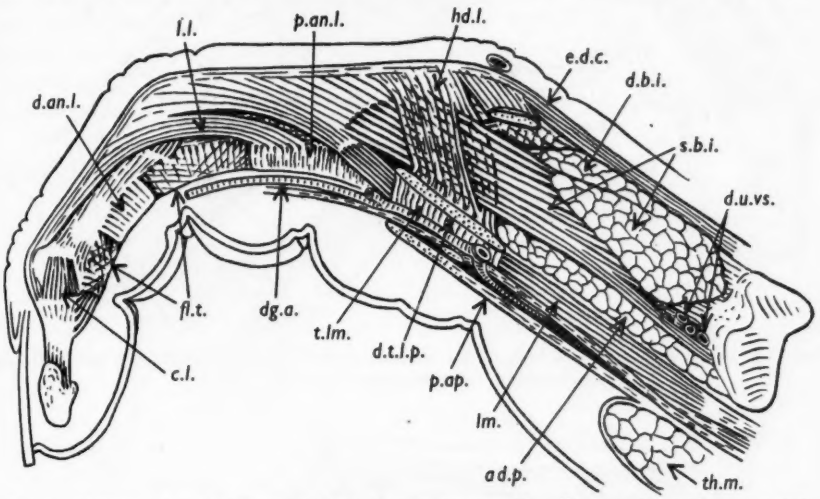

Fig. 5. Dissection of middle finger to show the extensor assembly. For lettering see key on p. 259.

diagram (fig. 5A), which shows the bellies combined nearly as far as their insertion, nor with Braithwaite *et al.* (1948, fig. 1). Salsbury (1937, p. 395) has pointed out that if a single-bellied interosseous muscle were inserted into the proximal phalanx it could not act as an extensor of the middle or distal joints. But as, in fact, the muscle splits distally into two distinct bellies Salsbury's difficulty does not arise. The partial subdivision of the interossei has been described before, and it has even been suggested that three muscles should be recognized in each intermetacarpal space (review and literature in Forster, 1916).

The palmar pad (*p.p.*) of the metacarpo-phalangeal joint is a mass of dense fibrous tissue with closely interwoven bundles of collagenous fibres, and is not a fibro-cartilage as suggested in some text-books. It is held in place by a pair of collateral ligaments of the pad (*c.l.p.p.*), adjacent to, but distinct from, the collateral ligaments of the joint (*c.l.*), and by the well-known distal attachment to the base of the proximal phalanx. The pads of adjacent digits are attached together by the deep transverse ligaments of the palm, made of ordinary ligamentous tissue. The distinction between pads and ligaments is an old one, but Braithwaite *et al.* (1948, p. 187) have reverted to the description of the whole mass of pads and ligaments as a single structure, their

deep transverse palmar ligament or deep intermetacarpal ligament, the latter a most inappropriate term as the structure is not directly attached to the metacarpal bones. The structure of the corresponding pads and ligaments of the foot has been discussed in some detail by Haines (1947).

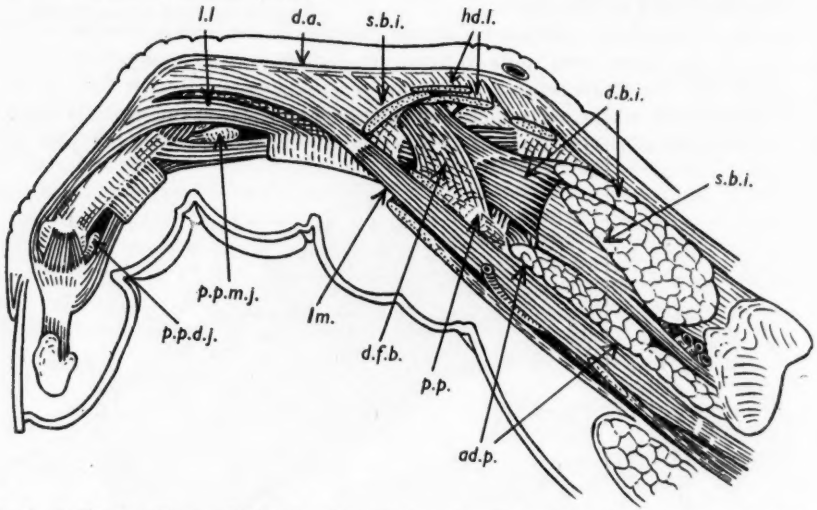

Fig. 6. As Fig. 5, with superficial belly of interosseous cut away and the fibrous flexor and lumbrical tunnels opened. For lettering see key on p. 259.

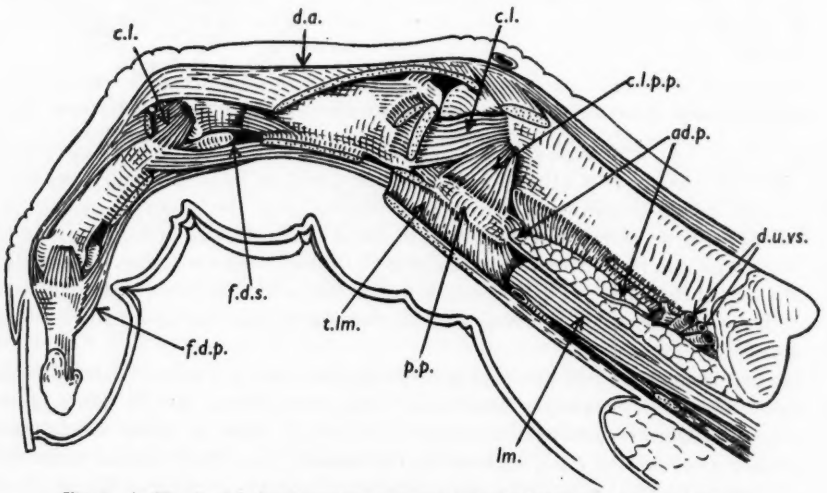

Fig. 7. As Fig. 6, with deep structures exposed. For lettering see key on p. 259.

In the region of the metacarpo-phalangeal joint the extensor apparatus is represented by the so-called 'dorsal expansion'. Attached to either side of this expansion is a sheet of transversely running fibres, the two sheets forming with the expansion

the 'transverse metacarpophalangeal fascia' of Salsbury (1937, p. 401), the 'dossière' of Montant & Baumann (1937, p. 314) and the 'extensor hood' of Braithwaite *et al.* (1948, p. 187). Since, however, the transverse fibres are distinct from the longitudinal fibres it seems better to break up the structure into a hood ligament on either side, and an extensor tendon passing distally into an extensor aponeurosis.

Each hood ligament is attached at its volar end to the palmar pad of the proximal joint, a point first stated clearly by Braithwaite *et al.* (1948, p. 187), though Salsbury (1937, p. 402) had already seen a well-defined band passing between the palmar edge of the interosseous and the side of the joint capsule. The ligament splits to enclose the interosseous muscle to which it is closely bound, particularly distally where the muscle is becoming aponeurotic. Another fibrous band (*d.f.b.*) is sometimes found passing to the phalanx between the hood ligament and the deep insertion of the interosseous. The fibrous tunnel for the lumbrical (*t.lm.*) is attached dorsally to the palmar pad and deep transverse ligament, and through it the palmar aponeurosis

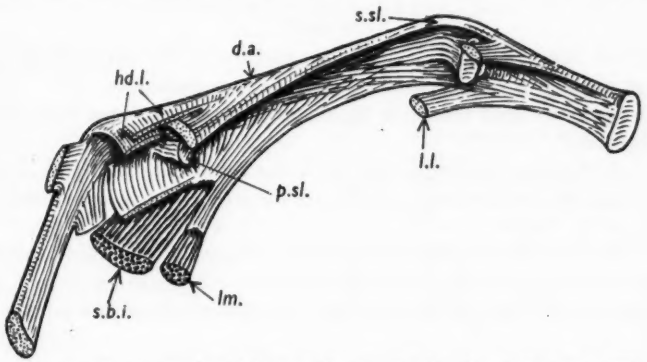

Fig. 8. Dorsal aponeurosis and its appendages. For lettering see key on p. 259.

(*p.ap.*) is firmly attached to the palmar pad (cf. Grodinsky & Holyoke, 1941). Thus opposite the metacarpal head a continuous series of strong fibrous structures attaches the extensor tendons to the palmar aponeurosis.

These various bands presumably serve to maintain the extensor tendon, the interossei and the palmar pad in place, particularly, as suggested by Salsbury (1937), to prevent the interossei moving too far away from the axis of the proximal joint when that joint is flexed, and so losing their power of extension at the middle and distal joints, but their action is not yet fully understood. Bunnell's suggestion (1942, p. 12 and fig. 8C) that the hood ligaments are necessary to give the interossei a purchase on the proximal phalanx and so allow them to flex the proximal joint, is inacceptable, for the interossei are not directly inserted into the ligaments.

A slip passes from the deep surface of the extensor tendon to the dorsum of the proximal phalanx near its base (*p.sl.*). This slip has been fully discussed by Hauck (1923) and Duensing (1944), and is very clearly figured by Bunnell (1942, fig. 5B), but recently Sunderland (1945, p. 196) found only a loosely arranged band of deep fibres. In most individuals, however, the slip is strong and well defined, though since it is slack in all positions of the proximal joint except in full hyperextension its

presence does not normally interfere with the action of the common extensor on the more distal joints.

The drawings of Hauck (1923, fig. 7A), Bunnell (1942, fig. 5A) and Duensing (1944, fig. 1) all show an insertion of some fibres of the interossei and lumbrical directly into the middle phalanx with the middle slip of the extensor aponeurosis, as well as a main insertion, through the side-slips of the aponeurosis, into the terminal phalanx. Braithwaite *et al.* (1948, fig. 1) show no such insertion, and state (p. 187) that the muscles join the side slips of the aponeurosis after these slips have diverged from the central insertion into the middle phalanx. My own work confirms that of the earlier authors, for in fact all the muscles inserted into the dorsal aponeurosis are bound together on the dorsum of the proximal phalanx. So whatever their action on the proximal joint all the muscles inserted on the aponeurosis must have the same actions on the middle and distal joints. This agrees well with the clinical and physiological conclusions of Duensing (1944) and Sunderland (1945).

SUMMARY

1. A pair of link ligaments attached proximally to the sides of the proximal phalanx and distally to the extensor aponeurosis is described.

2. These ligaments limit flexion in the distal joints of the finger when the middle joint is extended.

3. This linked motion combines with the volar shift of the side slips of the dorsal aponeurosis and with the ligamentous action of the interossei to give smooth combined movements of the digits.

4. Some details of the extensor assembly are reviewed, particularly the insertions of the interossei, the hood ligaments and their attachments to the palmar pads, and the insertion of some fibres of the interossei and lumbricals on the middle phalanx.

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The author deeply regrets his failure to consider the important recent paper by Landsmeer, J. N. F. (1949), 'The anatomy of the dorsal aponeurosis of the human finger and its functional significance', *Anat. Rec.* **104**, 31–44. Landsmeer's 'oblique band of the retinacular ligament' is the structure here referred to as the link ligament.

KEY TO LETTERING

ad.p.	adductor pollicis	*hd.l.*	hood ligament
c.l.	collateral ligament	*l.l.*	link ligament
c.l.p.p.	collateral ligament of palmar pad	*lm.*	lumbrical
d.a.	dorsal aponeurosis	*p.ap.*	palmar aponeurosis
d.an.l.	distal annular ligament	*p.an.l.*	proximal annular ligament
d.b.i.	deep belly of interosseous	*p.p.*	palmar pad
d.f.b.	deep fibrous band	*p.p.d.j.*	palmar pad of distal joint
dg.a.	digital artery	*p.p.m.j.*	palmar pad of middle joint
d.t.l.p.	deep transverse ligament of palm	*p.sl.*	proximal slip
d.u.vs.	deep ulnar vessels	*s.b.i.*	superficial belly of interosseous
e.d.c.	extensor digitorum communis	*s.sl.*	side slip
f.d.p.	flexor digitorum profundus	*t.lm.*	tunnel for lumbrical
f.d.s.	flexor digitorum sublimis	*th.m.*	thenar muscles
fl.t.	flexor tunnel		

p-s, l-o, and w-z in Figs. 1 and 3 are explained in the text.

OBSERVATIONS ON THE PRE-NATAL DEVELOPMENT OF THE INTERVERTEBRAL DISC IN MAN

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INTRODUCTION

This paper is concerned primarily with the pre-natal development of the intervertebral discs, but a series of discs at various ages after birth has been examined also for comparison. The development of the discs is intimately associated with that of the vertebral bodies and of the notochord. In the studies on the development of the vertebral column in man by Bardeen & Lewis (1901), Bardeen (1905, 1910), Müller (1906), Ask (1941), Reiter (1942), Wyburn (1944) and Sensenig (1949), and in the ox by Froriep (1886), in the white rat by Weiss (1901), in the mouse by Dawes (1930) and in the deer-mouse by Sensenig (1943), it is the vertebrae rather than the intervertebral discs that are chiefly dealt with.

The notochord has been studied as an independent structure in considerable detail by Schaffer (1930), and Prader (1945) has studied this structure in human embryos, while Williams (1908) studied its later development in mammals and included two references to human embryos.

The structure of the intervertebral disc at certain isolated pre-natal stages is referred to by Smith (1931), Keyes & Compère (1932) and Töndury (1947). Prader (1947*b*) gives a detailed account of the histogenesis of the peri-notochordal tissues in man, Luschka (1858) describes some embryonic stages of the human disc, while Carlier (1890) gives a detailed account of the development of the intervertebral disc in the sheep. Detailed studies of the human adult disc have been made by Fick (1904), Petersen (1930), Beadle (1931) and Coventry, Ghormley & Kernohan (1945*a*, *b*). The vascularization of the human disc has been studied by Übermuth (1929) and Böhmig (1930).

An examination of the literature just cited shows that there is no contribution dealing particularly with the development of the intervertebral disc, and apart from Prader's work (1947*b*), only references to pre-natal stages are scattered throughout the literature.

The present investigation was undertaken to determine, by the examination of a range of human embryos, the various stages in the histogenesis of the components of the disc, to ascertain the part played by the notochord in the formation of the nucleus pulposus, to study the relationship of the cartilage plates to the components of the disc and to make some observations on the vascularization of the developing disc.

MATERIALS

A closely graded series of thirty-eight human embryos and foetuses ranging from 3 mm. to full-term, and cut in coronal, horizontal, or sagittal planes, has been studied.

DESCRIPTION OF SPECIMENS

The specimens described are selected as showing well-marked stages of differentiation of the disc tissue.

8 mm. embryo cut in the coronal plane (Pl. 1, fig. 1)

This embryo shows the presence of mesodermal somites, bounded by intersegmental vessels. The myotomes are composed of large, heavily staining cells, a myocele is present, and the medial part of the somite is occupied by smaller cells, which are seen migrating towards the notochord. The cells are densely packed in the sclerotome, but are looser in the region of the notochord. An intrasclerotomic fissure of v. Ebner (1888) divides the sclerotome into anterior and posterior parts, but there is as yet no difference in cell density in these.

Although not seen in the photograph, the notochord is clearly defined and is composed of polygonal cells. No definite notochordal sheath is present, but there is a mesodermal sheath of several layers of cells.

7·5 mm. embryo cut in the horizontal plane (Pl. 1, fig. 2)

A marked distinction is seen in this embryo between the loosely and densely arranged cells of the sclerotomes, the two being disposed cranially and caudally respectively of the intrasclerotomic fissure. The notochord is well defined. The developing vertebral column is still in the blastemal stage.

10 mm. embryo cut in the coronal plane (Pl. 1, fig. 3)

Chondrification is present in the vertebral bodies in this embryo. The notochord is of uniform diameter throughout and is situated somewhat ventral to the central axis of the developing vertebral column. The notochordal cells are numerous, closely aggregated and clearly defined. There is a peri-notochordal thickening of several layers of mesodermal cells.

The area of the future disc shows dense mesodermal tissue. The cells are long oval and are arranged in concentric lamellae. In the coronal plane, the intrasclerotomic fissure may still be recognized; the tissue of the disc is related to the fissure so that one-third is cranial to it and two-thirds caudal. In the thoracic region, in horizontal sections, at the ventral edge of the disc, several rows of closely aggregated cells are seen which pass laterally to merge with the mesodermal head of the corresponding rib. This cell aggregation represents the hypochordal bow. Similar conditions are found in the 13 and 14 mm. embryos.

15 mm. embryo cut in the sagittal plane (Pl. 2, figs. 4, 5; Text-fig. 1)

Significant changes are present in this embryo. The notochord can be traced from basis cranii to coccyx. The developing vertebral bodies are formed of embryonic cartilage. The discs are slightly thicker at the circumference than at the centre. As seen in sagittal section (Pl. 2, fig. 5) the densely aggregated circumferential mesodermal cells run in fairly parallel rows between one vertebra and the next. The cells of the disc become more rounded as they are traced towards the centre and are irregularly arranged round the notochord. They have more intercellular substance between them than in the case of the vertebral bodies. This tissue towards the centre of the disc

Text-fig. 1. At 15 mm.

Text-fig. 2. At 29 mm.

Text-fig. 3. At 60 mm.

Text-fig. 4. At full term.

Text-fig. 1–4. Diagrammatic representation of differentiation of the tissues of the disc.

resembles cartilage, indeed indications of actual cartilage capsules are seen at various places, and it will be referred to as 'specialized embryonic cartilage' (Text-figs. 1–3).

The above features are seen throughout the vertebral column. No vascularization of the developing vertebral bodies or of the discs is seen. Conditions in the 16 and 17 mm. embryo are similar.

21 *mm. embryo cut in the sagittal plane* (Pl. 2, figs. 6. 7)

In this embryo further changes are present, especially in the notochord. The vertebrae are formed of embryonic cartilage. The notochord can be followed from the basis cranii to the coccyx, and it shows slight expansions in the intervertebral regions and constrictions in the vertebral bodies, in some of which only a tract of homogeneous, acellular material marks its site. Furthermore, the whole notochord follows a slightly undulating course, with slight dorsal convexities in the intervertebral regions and ventral convexities in the vertebral bodies. At various points in the lumbar region, small processes of notochordal tissue project from the main structure and pass dorsally in the vertebral bodies.

The intervertebral discs show similar characteristics throughout the embryo. They are biconcave, and are composed, from the circumference to the centre, of mesodermal tissue, 'specialized embryonic cartilage' and notochord.

In paramedian sagittal sections of the circumferential area of the intervertebral disc, three zones are visible (Pl. 2, fig. 7*a–c*). The middle zone of dense mesodermal tissue (*b*) is the disc and the zones *a* and *c*, the cartilage plates.

No vascularization of vertebral bodies or discs is present. Similar features are seen in embryos of 22–25 mm.

26 *mm. embryo cut in the coronal plane* (Pl. 2, fig. 8)

In this embryo the disc shows, from without inwards, mesodermal cells, 'specialized embryonic cartilage', in which cell capsules can be seen, and the notochord.

29 *mm. embryo cut in the sagittal plane* (Pl. 2, fig. 9; Text-fig. 2)

In this embryo pronounced changes are present in the tissue of the notochord. The notochordal expansions and constrictions are somewhat more defined, the sheath being thickened in the intravertebral areas. In the notochord itself, spaces have appeared between the cells, and these spaces contain a homogeneous, slightly basophil substance. The separation of some groups of cells and compression of others gives the appearance of a network-like tissue, referred to as the 'chorda-reticulum'.

At the circumference of the disc definite fibres are now present, and this part of the disc may now be truly termed the annulus fibrosus. These fibres, running in parallel rows, cross the intervertebral space and their terminations are lost in the adjacent vertebrae. The innermost fibres are only half as long as the outermost; some of the fibres are seen to run obliquely and the disc as a whole is biconcave. The specialized peri-notochordal cartilage is well seen. Enlargement of intravertebral peri-notochordal cartilage cells indicates the preliminary stages of ossification. The cartilage at the ends of the vertebral bodies into which the fibres pass, stains more lightly with haematoxylin than that of the bodies themselves, and along the boundaries of the intervertebral spaces the cartilage cells are flattened and arranged

Text-fig. 1–4. Diagrammatic representation of differentiation of the tissues of the disc.

in horizontal rows. These areas are the cartilage plates which serve to anchor the fibres of the disc, and which by proliferation of cells, are responsible for the growth of the vertebrae in height. No vascularization of vertebral bodies or discs is present. In a specimen of 30 mm. well-developed obliquely running fibres are also present in the annulus fibrosus.

47 *mm. embryo cut in the horizontal plane* (Pl. 3, figs. 10, 11)

The notochord has expanded in a transverse direction. The peri-notochordal cartilage, dorsal to the notochord, shows a looser arrangement of its cells and more intercellular substance than similar tissue ventral to the notochord. This loosening of tissue appears to precede a dorsal expansion of the notochord. Well-defined fibres are present in the annulus.

60 *mm. embryo cut in the sagittal plane* (Pl. 3, fig. 12; Text-fig. 3)

Centres of ossification are well defined in the vertebral bodies. The notochord has expanded in a dorsal direction and remnants only of the notochordal sheath are seen, near the upper and lower surfaces of the intervertebral discs. The notochordal cells are polygonal and vesicular, with large, heavily staining nuclei, the cytoplasm staining lightly with Biebrich's Scarlet. Spaces containing a lightly staining, amorphous, basophil substance are present between the cell groups, and in some regions a chorda-reticulum is present. More peripherally in the notochordal area, rows of cartilage cells are seen in an abundant matrix, those nearest the notochord encircle it and then pass to mingle with the cartilage of the vertebral bodies. A little further peripherally, the matrix is abundant and the cells run in parallel rows, with an outward convexity like that of the fibres of the annulus, seen still more peripherally. In tracing the tissues from the notochordal area to the circumference, there is a transition from the peri-notochordal cartilage to fibrocartilage and finally to the fibres of the annulus.

This succeeding tissue differentiation suggests that the peri-notochordal specialized embryonic cartilage is forming the future fibrocartilaginous component of the disc, and may contribute to the inner area of the annulus fibrosus. The fibres of the annulus are again seen to terminate in the cartilage plate. As regards vascularization of the vertebrae, vascular channels are present peripherally at the level of a plane passing between the vertebral body and the cartilage plate, while dorsally in the vertebral body a depression containing blood vessels is seen at the site of the definitive foramina for the basivertebral veins. No vascularization of the notochordal area or of the annulus fibrosus is present.

99 *mm. embryo cut in the horizontal plane* (Pl. 3, fig. 13)

In this embryo the notochordal area is seen expanded, with a chorda-reticulum and intercellular spaces containing a homogeneous substance, while more peripherally is the fibrocartilage zone, and beyond this the concentric fibres of the annulus fibrosus. Ventrally, at the circumference of the annulus, a dense fibre concentration is present, and ventral to this again there are fibres of the anterior longitudinal ligament. The annulus shows splitting and joining of the fibres of different lamellae and an interlocking of the various lamellae.

Among the peripheral fibres of the annulus a few small blood vessels are present in the dorsolateral areas of the disc, but there is no vascularization of the inner part of the disc nor of the notochordal area.

150 *mm. embryo cut in the sagittal plane* (Pl. 3, fig. 14)

In paramedian sagittal sections of this specimen the complicated architecture of the fibre system of the annulus fibrosus is particularly well seen.

210 *mm. embryo cut in the sagittal plane* (Pl. 3, fig. 15)

In this embryo the principal change is in the notochordal area. This has enlarged, and in a median sagittal section is elongated ventro-dorsally to occupy half the length of the intervertebral region. It contains a faintly basophil, structureless substance, in which groups of notochordal cells are present. These are much reduced in number and some show heavily staining, rounded nuclei, while in others the nuclei are pyknotic. The remains of a chorda reticulum are present. Passing from the notochordal area to the circumference, we see the peri-notochordal cartilage with its cells arranged in rows, forming a capsule for the notochord, then the fibrocartilage and finally the fibres of the annulus.

The vascularization is as seen in the 99 mm. specimen.

The full-term foetus cut in the sagittal plane (Pl. 4, fig. 16; Text-fig. 4)

In this specimen, centres of ossification are present in the vertebral bodies; bony trabeculae are developed, and marrow occupies the intertrabecular spaces. The vertebral bodies are capped above and below with cartilage, which in the intervertebral area receives the fibres of the annulus and the fibrocartilaginous component. No vestige of notochord is present in the vertebral bodies.

In a median sagittal section the notochordal area is extensive, somewhat biconvex, and occupied by a faintly basophil, homogeneous substance, in which the remains of a chorda reticulum are present. Here and there are small groups of recognizable notochordal cells. At the circumference of the notochordal area collagenous fibres and cartilage cells are to be seen, embedded in the homogeneous, mucoid substance. These appear to be derived from liquefaction in the inner part of the fibrocartilaginous zone which surrounds the notochordal area. External to this zone is the annulus fibrosus. Vascular canals are present, as in the previous specimen, but no vessels are seen to enter the notochordal area. A few small vessels run between the lamellae of the annulus but are confined to the dorsolateral areas.

The ventral part of a disc of a full-term foetus, seen in horizontal section (Pl. 4, fig. 17), shows the architecture of the fibre system. To the right of the figure are seen the fibres of the anterior longitudinal ligament, deep to which are several very dense lamellae representing the contribution to the disc from the hypochordal bow. The intricate splitting and interlocking of the various lamellae are evident, and the whole structure of the annulus fibrosus resembles that of the adult.

Examination of a series of post-natal human intervertebral discs, ranging in decades from birth to 80 years of age, shows a progressive invasion of the notochordal area by collagenous fibres and cartilage cells, ultimately resulting in the complete transformation of this area to fibrocartilage. These elements are derived from the

fibrocartilaginous zone of the disc, which in turn is derived from the peri-notochordal specialized embryonic cartilage. It may be noted that until transformation of this latter tissue occurs, the vertebral bodies are in cartilaginous continuity. Müller (1906) refers to this but does not describe the specialized character of the connecting cartilage.

The term nucleus pulposus is employed to designate the macroscopically gelatinous, apparently structureless, semi-fluid mass contained within the annulus fibrosus of the pre- and post-natal disc. The structure of the nucleus pulposus before birth is mainly notochordal and after birth, modified as described above. Thus, one term is employed to designate areas having similar sites but different histological structure. The difficulty could be overcome by the use of the terms 'pre-natal' and 'post-natal' nucleus pulposus.

REVIEW OF OBSERVATIONS AND DISCUSSION

(1) *Preliminary developmental changes*

The developmental changes of the human vertebral column are referred to by Bardeen (1905) as blastemal, chondrogenous and osseogenous, and though overlapping of these periods occurs, this classification adequately summarizes the main developmental phases.

In early stages the sclerotome is divided by the fissure of v. Ebner (1888) into a cranial and a caudal half with a loose cell aggregation in the former and a dense cell aggregation in the latter.

From the observations made in the present investigation, and by Remane (1936), Reiter (1942), Prader (1947*a*) and Sensenig (1949), the densely aggregated tissue is found after the 6 mm. stage both cranial and caudal to the fissure of v. Ebner, occupying the caudal third of the cranial half-sclerotome and the cranial two-thirds of the caudal half-sclerotome (see Pl. 1, fig. 3). This condensed tissue forms the *anlage* of the intervertebral disc, which therefore receives contributions from both cranial and caudal half-sclerotome. Bardeen (1905) refers to the 'primitive disc' as being strengthened anteriorly by a condensation of tissue bounding the fissure of v. Ebner, while Prader (1947*a*) considers that the condensed tissue, at first limited to the caudal half-sclerotome, 'migrates headwards' and forms the *analage* of the primitive intervertebral disc. From this it may be assumed that while the disc is formed by contributions from both half-sclerotomes, the major contribution is from the posterior half-sclerotome.

(2) *The annulus fibrosus*

This is developed from the dense tissue described above. At first the mesodermal cells are rounded and do not show any specific arrangement, but by the 10 mm. stage the cells have become elongated, and in transverse sections of the disc show evidence of concentric arrangement. From this time onwards there is a thickened band consisting of several layers of cells, which connects the costal elements of both sides across the front of the disc. This band can be identified at all subsequent stages and evidently represents the hypochordal bow of Froriep (1886) which is subsequently added to, and forms a component of, the intervertebral disc. Further elongation of the mesodermal cells follows, and by the 29 mm. stage fibres are present and con-

centric lamellae are well defined. By 38 mm. oblique fibres are well developed. These fibres run a spiral course from one vertebra across the intervertebral space to the next. Crossing of different sets of fibres, in some instances, occurs at an angle of almost 90°.

The annulus fibres bound an area of peri-notochordal specialized embryonic cartilage. As histogenesis proceeds, it may be observed that the most peripheral part of the disc is composed of closely aggregated fibres, while the inner part shows a more open tissue. It has been suggested by Prader (1947*b*) that the peri-notochordal cartilaginous area contributes to the inner part of the annulus. From 60 mm. onwards, fibrocartilage makes its appearance between the fibrous annulus and the narrow area of cartilage that surrounds the notochord and persists almost to the time of birth. In the full-term foetus, this cartilage has differentiated into fibrocartilage, and so far as the annulus is concerned, the definitive condition exists.

The attachment of the disc to the cartilage plate is effected by the termination of the disc fibres among the cartilage cells of the adjacent vertebrae previously referred to. The fibre constitution of the disc is denser ventrally than dorsally, and the connexion of the annulus to the anterior longitudinal ligament is more intimate than to the posterior longitudinal ligament.

Some reference may be made to the thickness of the disc *anlage*. In the somite stage as seen in sections in the coronal and sagittal planes, the dense tissue has the same thickness as the loose tissue. When chondrification of the vertebrae occurs, the disc becomes thinner, but the upper and lower surfaces are flat. By the 15 mm. stage viewed in median sagittal section, the disc is biconcave and this condition persists till birth.

The annulus fibrosus is the first component of the disc to show a definite cellular arrangement, and it achieves its highly complex architecture long before movement or any stress occurs in the vertebral column. It is fully differentiated at birth. Examination of adult discs shows that the structure of the annulus fibrosus remains unchanged for many years.

(3) *The notochord*

In the 3 mm. embryo, the notochord in the cranial region of the blastemal vertebral column is circular in outline and presents the suggestion of a canal in its lumen. His (1880) records a distinct lumen in an embryo of 2·4 mm. No definite lumen is seen in the notochord of other embryos in this series. In the caudal region, the notochord in the early stages is somewhat flattened and approaches the developing neural tube. Bremer (1906) describes similar features in a 4 mm. embryo and states that not far from the end of the tail, 'the notochord is lost by merging with the spinal cord'. Sensenig (1949) describes contact of the notochord with the neural tube in embryos up to 3·7 mm. This feature is not seen in the present series of embryos.

At the 10 mm. stage the notochord has a uniform diameter throughout, but by the 21 mm. stage, it shows an intravertebral narrowing and slight intervertebral fusiform expansion. These two parts of the notochord are referred to by Schaffer (1910) as 'Chordascheidenstrang' and 'Chordasegment' respectively. In the 26 and 29 mm. specimens, the intervertebral expansion is more pronounced. At 47 mm. the intervertebral notochord has passed from the spindle-like form of the 21 mm. stage, to that of an oval structure about as broad as it is long, while in the intravertebral region, a narrow tract of homogeneous, acellular substance representing the noto-

chordal sheath is seen. At 60 mm. the notochord has expanded dorsally, as is also seen in the 93, 99 and 156 mm. stages, and by full term the notochordal area occupies a considerable proportion of the total area of the whole disc. In the 99 mm. embryo, in following serial sections through the disc from above downwards, at first a circular notochord is seen, then the dorsal expansion appears, while the rounded ventral part of the notochord is still visible, the whole area being key-hole shaped. At the same time the notochord expands laterally.

Böhmig (1930) considers the forms of intervertebral notochord as so characteristic that he designates them as 'Rhombusform', 'Pilzform', 'Stabform', 'Dachform' and 'V-form' and figures all types in his 86 mm. embryo. No such defined forms are seen in the series here investigated.

Schaffer (1910) and Prader (1945) consider the alterations in the form of the notochord to be due to cranial and caudal pressure which is responsible for the broadening and shortening, while the dorsal convexity of the embryo permits dorsal extension.

The position of the notochord relative to the central axis of the vertebral column demands consideration. In the early stages, it runs approximately centrally through the developing column (except as noted in the caudal extremity), but at 10 mm. it is slightly more ventrally placed and it retains this position during foetal life. When the cartilage cells at the centre of the developing vertebral body enlarge as a preliminary to ossification, the notochord passes through the ventral part of this area. When ossification occurs, the notochord maintains its position, and is represented for a time by the notochordal sheath until this disappears in later stages.

In the adult, the nucleus pulposus is situated in the dorsal part of the disc. This is accounted for by the fact that the disc and vertebral body do not increase in size concentrically. The peri-notochordal component of the disc increases more in a ventral than in a dorsal direction, and growth of the vertebral body occurs by accretion at the ventral surface, as has been shown by the radiological studies of Knutsson (1948).

The intervertebral expansion of the notochord begins at 21 mm. and thereafter is progressive. The cells in the intervertebral area increase in number, while those in the intravertebral area decrease. The question arises, as to whether there is degeneration of the intravertebral cells and proliferation of the intervertebral cells, or whether mere passive displacement of the cells occurs. Schaffer (1910) considers the mechanism to be one of passive displacement, a view previously held by Kölliker (1879). Estimation of the total number of cells shows that this remains the same. Mitoses are recorded by Prader (1945) up to the 3·5 mm. stage, but not later. Schaffer (1910) isolated notochordal cells in the fresh state, and found them to be vesicular, pressure-resisting and capable of displacement. Hence, the production of notochordal expansions may be due to pressure exerted on the notochord by the increasing chondrification of the vertebral bodies, resulting in the displacement of the notochordal cells to the intervertebral region.

Remains of notochordal cells, or elongated cells, are to be found occasionally in the notochordal sheath near the intervertebral region, where tissues are more yielding. Rarely, notochordal tissue persists in the intravertebral region, into adult life, as recorded by Musgrove (1891) and Schmorl (1928).

Another feature is the occurrence of segmental notochordal flexures. These have been described in the human embryo by Minot (1907), Schaffer (1910), Böhmig (1930), Prader (1945), and Sensenig (1949), and in the rabbit by Kölliker (1879) and Löwe (1879). The only comment on any part played by the flexures in relation to the disc is made by Carlier (1890) in reference to the sheep. He describes, in the lumbar region of an embryo of 1·25 in., a ventral intervertebral bending of the notochord, in the median sagittal plane; the curvature thus approaching the ventral surface of the column. In specimens examined just after birth, only the most ventral part of the intervertebral notochordal curvature persists to form the nucleus pulposus.

In the present series of embryos, segmental flexures of the notochord are seen in the lumbar region, in median and paramedian sagittal sections. At 15 and 21 mm. the curvatures are directed dorsally in the intervertebral region and ventrally in the intravertebral region. At 60 mm. there is evidence of a dorsally directed curvature in the intravertebral notochordal vestige, while the intervertebral notochord is so expanded that it cannot be related to any curvature.

Similar segmental flexures are illustrated by Böhmig (1930). The causation is obscure. Dursy (1869) suggests that they are due to excessive growth in length of the notochord, while Schaffer (1910) ascribes them to mechanical factors and the influence of the presence of ossification.

The sheath of the notochord in man is less complex than in lower vertebrates. Bardeen (1910) states that a sheath is present in the human embryo at the fourth week of intrauterine life (at approximately the 2·5 mm. stage). Linck (1911) does not describe a sheath till the 20 mm. stage, and Reiter (1942) describes a sheath in an embryo of 3·6 mm. Prader (1945) states that no sheath is present in his 3·5 mm. embryo but that a thin sheath is present from the 5 mm. stage onwards. Sensenig (1949) describes a thin homogeneous sheath in his specimens of 3–7·5 mm.

In the series of embryos investigated, a thin, amorphous sheath is first seen at 5 mm. and with the onset of chondrification of the column and the development of the notochordal expansions and constrictions, the sheath becomes progressively thinner intervertebrally and thicker intravertebrally. The sheath stains lightly with basic stains and though acellular shows a longitudinal striation and gives the impression of a fibrillar structure. Its appearance is very like that of the matrix of hyaline cartilage. At the 99 mm. stage a notochordal sheath seems to re-appear in the intervertebral region, and at the 210 mm. stage the notochordal cavity appears to be lined with a substance resembling the earlier sheath. At later stages it cannot be distinguished as a separate entity.

The part played by the notochord in the formation of the nucleus pulposus has been a matter of controversy. Certain authors (Gegenbaur, 1878; Hertwig, 1898; Williams, 1908) state that the nucleus pulposus is formed by the persistence of the notochord or increase of its cells, while others (Heiberg, 1880) consider that the notochord plays no part in its formation. The nucleus pulposus has been derived 'from a central growth of cartilage' (Virchow, 1857), or regarded as a secondary formation that develops by degeneration of the cartilage of the vertebral body in the intervertebral region (Weiss, 1901). Other authors merely record the presence of notochordal cells in the newborn (Löwe (1879) in the rabbit; Schaffer (1910) in the

human foetus). Wiedersheim (1897) states that in mammals the notochord persists longer intervertebrally than intravertebrally, but disappears entirely by the time the adult condition is reached. Luschka (1858) concludes that the nucleus pulposus is formed partly by notochordal changes and partly by liquefaction of the innermost layers of the matrix of the surrounding tissue, while Keyes & Compère (1932) consider that up till birth, the notochord forms the chief source of the nucleus pulposus. Linck (1911) concludes that the structural characteristics of notochordal cells indicate that they are not secreting cells, that the mucoid substance is intercellular, and is produced by mucoid degeneration of these cells.

The present investigation shows that the nucleus pulposus at birth is formed by notochordal tissue (Text-fig. 4), modified as described previously.

(4) *The early vascularization of the disc*

Böhmig (1930), from a study of human pre- and post-natal specimens ranging from 60 mm. to 30 years of adult life, states that all discs up to 25 years of age are supplied from six principal vessels, two dorsal, ventral and axial vessels. He states that these not only supply the 'intervertebral cartilage' of embryos, but also the cartilage plates of juveniles, and the annulus fibrosus and nucleus pulposus of later stages. He figures these vessels in his Plate 11. On examination of this Plate, the vessels can be seen, but they appear to be running in the cartilage plates and do not enter the nucleus pulposus. The Plates are all of microscopic sections, with a maximum magnification of 35·0 and hence a general view only is obtained.

Übermuth (1929) describes peripheral vessels in the cartilage plates only, while Smith (1931) reports the presence of 'nutritive channels' in the nucleus pulposus and in the annulus, in post-natal stages only.

In the present series, small vessels certainly run in the cartilage plates, and small vessels are found from 93 mm. onward, running in the peripheral lamellae of the annulus fibrosus only, and confined to the dorsal regions of this. These vessels are well seen at 150 mm. (Pl. 4, fig. 18). No vessels are seen to enter the nucleus pulposus, which remains avascular during foetal life.

SUMMARY

1. Descriptions are given of the development of the intervertebral disc in a series of pre-natal human specimens ranging from 3 mm. to full term. The points particularly noted are the histogenesis of the annulus fibrosus, the notochordal changes in relation to the formation of the nucleus pulposus, the peri-notochordal tissue, the relationship of the cartilage plates to the disc, and the vascularization of the disc.

2. The intervertebral disc develops from the densely aggregated mesoderm, early differentiated in the somite. This tissue is found at early stages on both sides of the fissure of v. Ebner and hence the disc receives contributions from both cranial and caudal half-sclerotomes.

3. At early stages the peri-notochordal tissue is formed by a 'specialized embryonic cartilage' which, for a time, connects the vertebrae so as to form a continuous cartilaginous column. This specialized cartilage later differentiates to form the fibro-cartilaginous component of the disc, and is a potential source of additions for the growth of the nucleus pulposus of post-natal life.

4. In foetal life, the nucleus pulposus is produced by a modification of the notochord, characterized by the mucoid degeneration of its cells, resulting in the progressive disappearance of notochordal cells and increase of mucoid substance. At birth a diminished number of notochordal cells is present. The notochord continually changes in structure, and after birth fibres and cartilage cells are added to the notochordal area, producing the post-natal nucleus pulposus. The use of the terms 'pre-natal' and 'post-natal' nucleus pulposus is suggested to indicate the change in structure described.

The alteration in position of the site of the foetal and adult nucleus pulposus within the disc may be due to the growth in girth of the discs and vertebrae being greater at the ventral surface.

5. The annulus fibrosus is differentiated very early in development, the mesodermal *anlage* showing differentiation at 13 mm. The intricate fibre system develops long before the vertebral column is subject to external mechanical influences. Well-defined fibres are present at 29 mm.

6. The annulus fibrosus is anchored, from its beginning, to the cartilage plates. The cartilage plates are developed by extension of chondrification from the vertebral body.

7. The vertebrae are freely vascularized during foetal life, and some vessels enter the cartilage plates.

8. The nucleus pulposus is avascular during foetal life, while the annulus fibrosus is vascularized only in its outer lamellae dorsally, and by very small vessels.

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List of abbreviations for the text-figure

A.F.	Annulus fibrosus	*M.S.*	Mucoid substance
B.T.	Bone trabeculae	*Nch.*	Notochord
C.O.	Centre of ossification	*Nch.C.*	Notochordal cells
C.P.	Cartilage Plate	*Nch.V.*	Notochordal vestige
F.C.	Fibrocartilage	*Sp.E.C.*	Specialized embryonic cartilage
F.T.	Fibrous tissue	*V.B.*	Vertebral body
Mes.C.	Mesodermal cells	*V.C.*	Vascular canal

EXPLANATION OF PLATES

PLATE 1

Fig. 1. 3 mm. (C.R.). Human embryo. Coronal section, showing myotome, sclerotome, intrasclerotomic fissure. Haematoxylin and Biebrich's Scarlet. ×1950.

Fig. 2. 7·5 mm. (C.R.). Human embryo. Horizontal section, region of basis cranii, showing notochord, loosely and densely arranged mesoderm of half-sclerotomes, intersegmental vessels. Haematoxylin and eosin. ×68.

Fig. 3. 10 mm. (C.R.). Human embryo. Coronal section, lumbar region, showing notochord, loosely and densely arranged mesoderm of half-sclerotomes, intrasclerotomic fissure. Haematoxylin and eosin. ×415.

PLATE 2

Fig. 4. 15 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing notochord, *anlagen* of vertebral bodies and intervertebral discs. Haematoxylin and eosin. ×75.

Fig. 5. 15 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing notochord, 'specialized embryonic cartilage', mesoderm cells. Haematoxylin and eosin. ×300.

Fig. 6. 21 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing intervertebral notochordal expansions and intravertebral constrictions, *anlage* of intervertebral disc, showing 'specialized embryonic cartilage' and peripheral mesodermal cells of developing annulus. Haematoxylin and eosin. ×60.

Fig. 7. 21 mm. (C.R.). Human embryo. Paramedian sagittal section, lumbar region, showing *anlagen* of vertebral bodies, and intervertebral disc (*b*) and *anlagen* of the cartilage plates (*a*, *c*). Haematoxylin and eosin. ×60.

Fig. 8. 26 mm. (C.R.). Human embryo. Coronal section, lumbar region, showing notochordal cells, 'specialized embryonic cartilage' and peripheral annulus mesodermal cells. Haematoxylin and eosin. × 500.

Fig. 9. 29 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing notochordal reticulum, intercellular spaces in notochord, 'specialized embryonic cartilage' and fibres now present in the annulus. Haematoxylin and eosin. × 75.

PLATE 3

Fig. 10. 47 mm. (C.R.). Human embryo. Horizontal section, lumbar region, showing notochordal expansion, intercellular spaces in notochord, perichordal cartilage, fibres of annulus and loose texture of cartilage dorsal to notochord. Masson's Trichrome. × 125.

Fig. 11. 47 mm. (C.R.). Human embryo. Horizontal section, lumbar region, showing notochord (*a*) and perichordal cartilage (*b*). Masson's Trichrome. × 300.

Fig. 12. 60 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing at the lower part of the figure, part of the notochordal cavity, above this the perichordal cartilage, succeeded by fibrocartilage and fibres of the annulus. Cartilage plates are shown receiving terminations of annulus fibres. Haematoxylin and Biebrich's Scarlet. × 100.

Fig. 13. 99 mm. (C.R.). Human embryo. Horizontal section, lumbar region, showing notochordal expansion, perichordal cartilage, fibrocartilage and fibres of the annulus. Masson's Trichrome. × 20.

Fig. 14. 150 mm. (C.R.). Human embryo. Paramedian sagittal section of annulus fibrosus from lumbar region, showing fibre architecture. Masson's Trichrome. × 100.

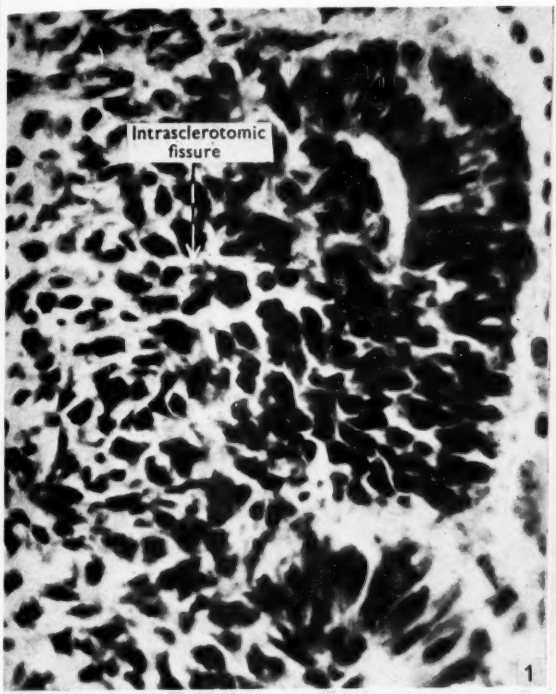
Fig. 15. 210 mm. (C.R.). Human embryo. Median sagittal section, lumbar region, showing notochordal cavity, containing few notochordal cells and abundant mucoid substance. Haematoxylin and eosin. × 50.

PLATE 4

Fig. 16. Full-term foetus. Median sagittal section, lumbar region, showing intervertebral area, notochordal cavity containing few notochordal cells and abundant mucoid material. Vertebral bodies and vascular canals are shown. Haematoxylin and eosin. × 16.

Fig. 17. Full-term intervertebral disc. Horizontal section, lumbar region, showing architecture of annulus fibrosus. The dense fibre concentration to the right of the figure is the hypochordal bow component. Haematoxylin and eosin. × 200.

Fig. 18. 150 mm. (C.R.). Human embryo. Parasagittal section, lumbar region, showing vessels in the dorso-lateral aspect of the periphery of the annulus fibrosus. Masson's Trichrome. × 100.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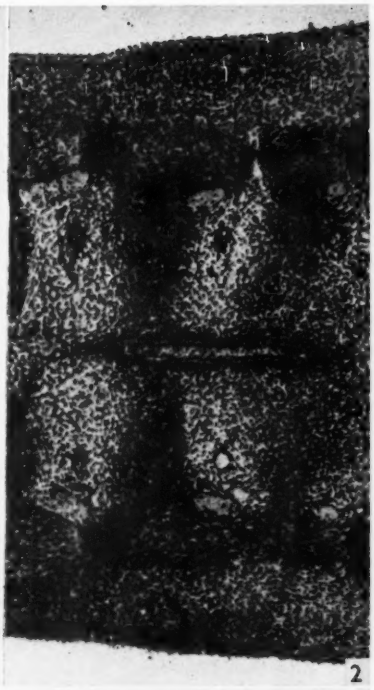
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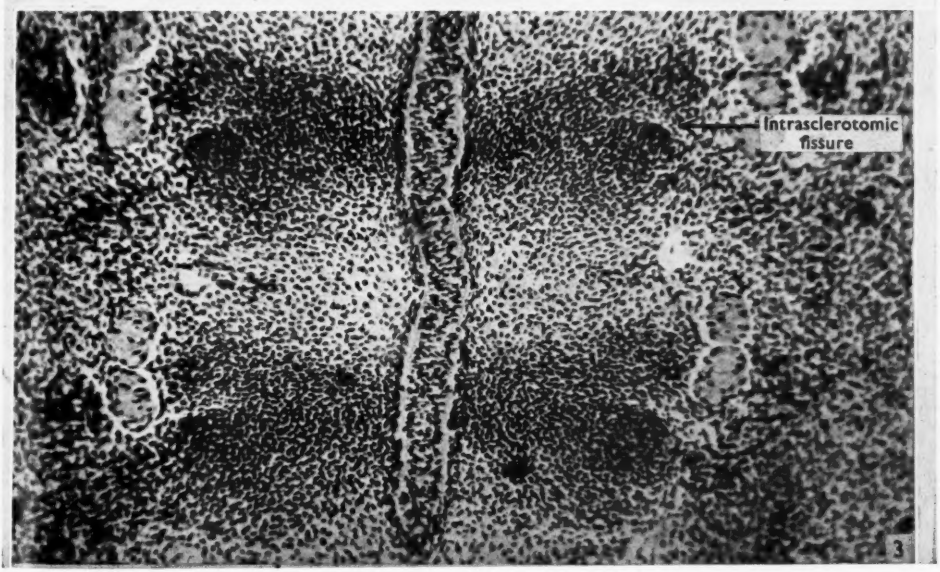
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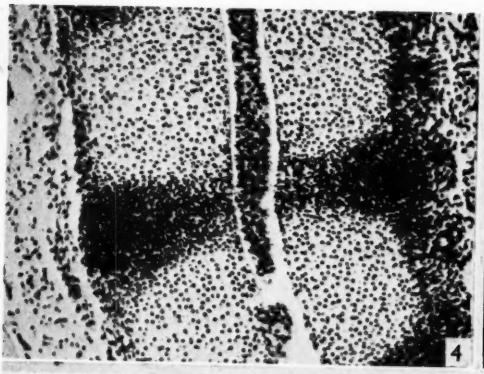
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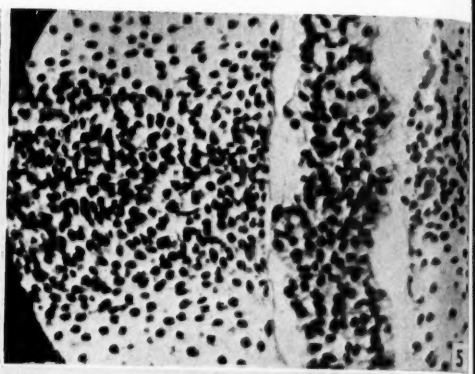
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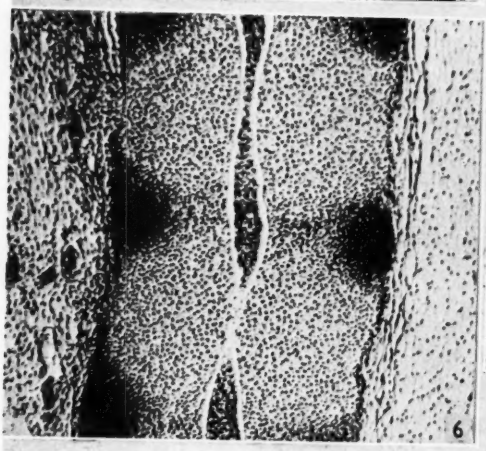
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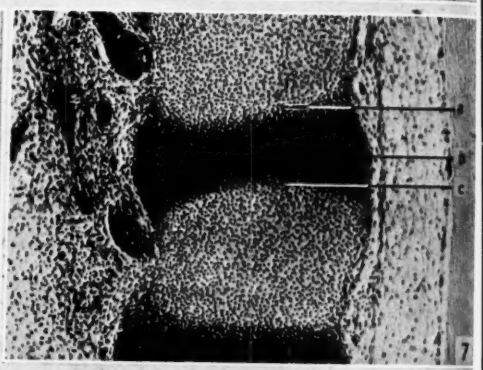
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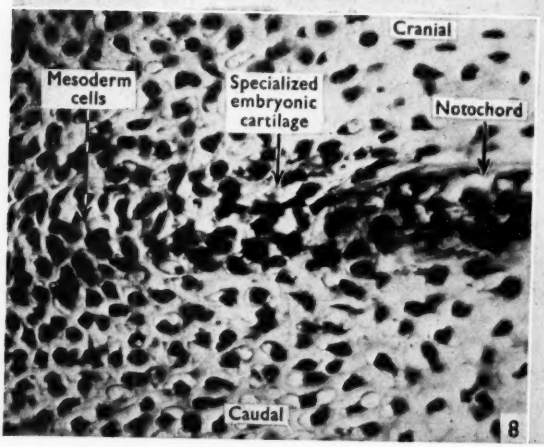
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Mesoderm cells
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Notochord
Caudal
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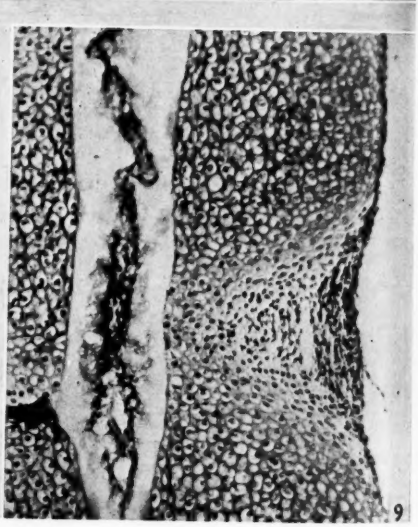
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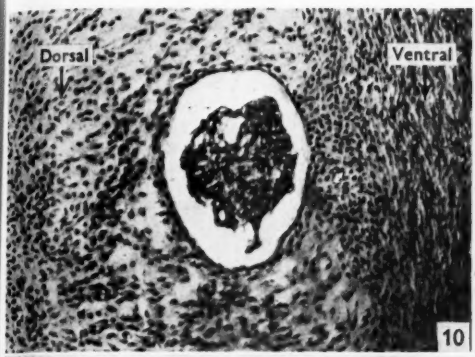
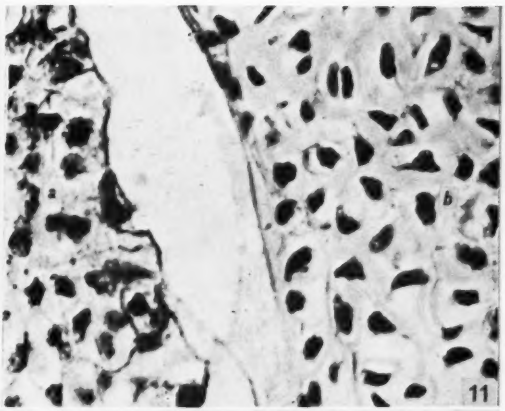
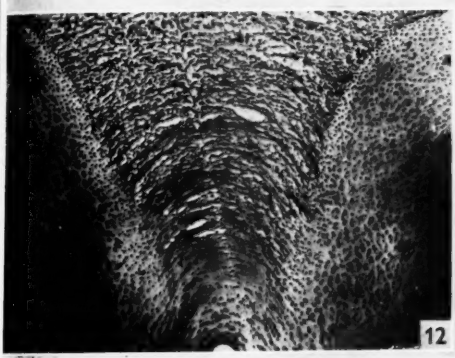
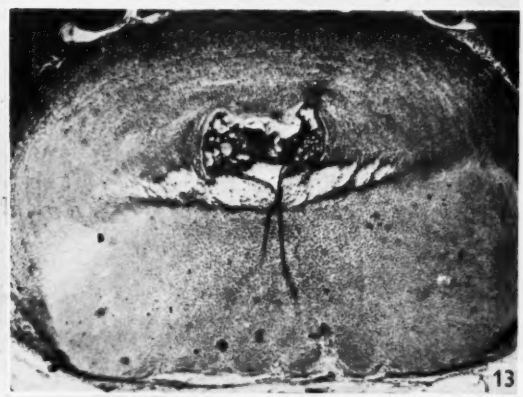
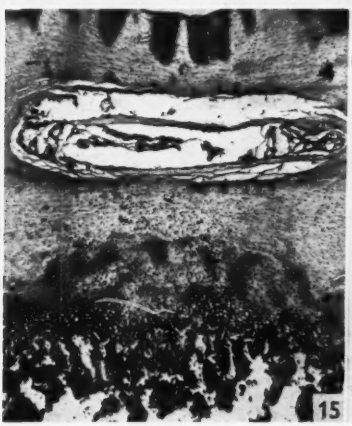


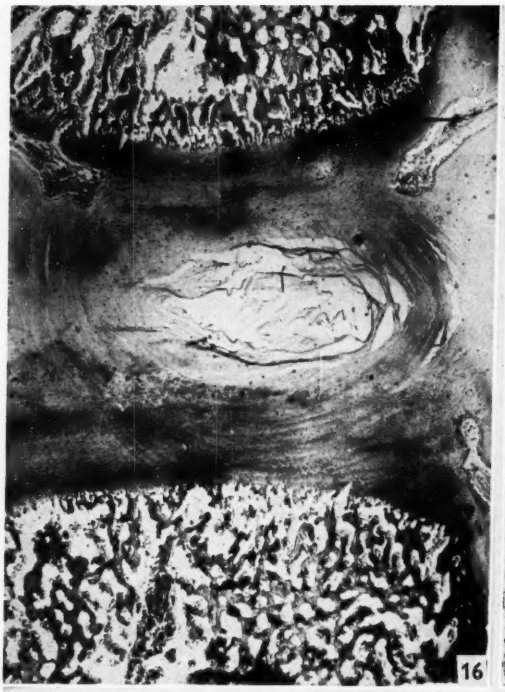


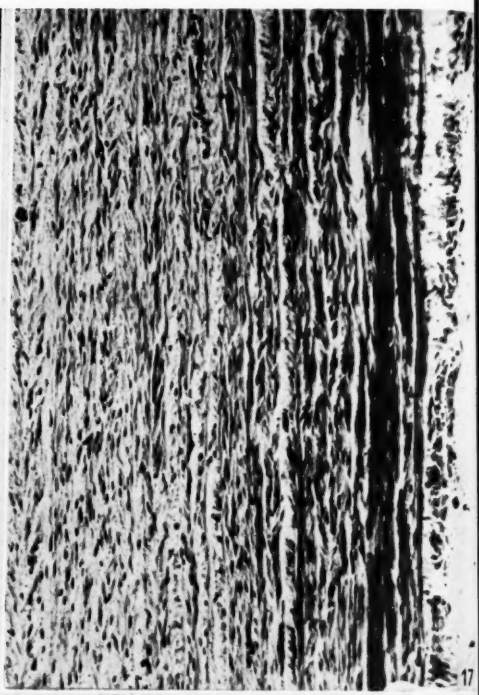






PEACOCK—PRE-NATAL DEVELOPMENT OF THE INTERVERTEBRAL DISC IN MAN





PEACOCK—PRE-NATAL DEVELOPMENT OF THE INTERVERTEBRAL DISC IN MAN

AN EXPERIMENTAL STUDY OF THE VISUAL PATHWAYS IN A SNAKE (*NATRIX NATRIX*)

J. A. ARMSTRONG

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Remarkably few investigations have been made on the detailed structure of the ophidian central nervous system. Apart from observations by Warner (1931, 1947) on the forebrain and midbrain of *Crotalus*, only sporadic references occur in the literature to the morphology of particular cell masses and fibre systems in certain snakes. Papers by Gross (1903) on the optic chiasma, by Huber & Crosby (1933) on the optic tectum and by Frey (1937) on the basal optic root are of special interest with regard to the visual system. However, little has been added to our knowledge of central optic connexions in the snake since the early treatise by Bellonci (1888), on the optic system in vertebrates, which included observations on *Natrix*.

Histological studies of the ophidian brain have so far been based almost exclusively on normal material. Gross (1903) used the Marchi technique in *Natrix* and other reptiles following the removal of an eye, but his results were entirely negative. Recently (Armstrong, 1950) experiments were described in which silver impregnation was used to demonstrate axonal and terminal degeneration as a method for the detailed analysis of the primary visual pathways of *Lacerta vivipara*. The results were encouraging, and the same method is now used for a similar investigation in the grass snake, *Natrix natrix*.

The subject is of particular interest in view of the theory recently offered by Walls (1942) that snakes originated from ancestral burrowing lizards in which the eyes had almost disappeared. Certain peculiarities of the ophidian eye were interpreted as evidence that the visual system in modern snakes has been reconstructed. If this is correct, one might expect to find some significant differences between the central visual pathways of snakes and of other reptiles; it seemed likely that any such difference between *Natrix* and *Lacerta* would be made apparent by the present experiments.

MATERIAL AND METHODS

The animals studied were British specimens of *Natrix natrix*. They were kept in boxes maintained at a temperature of 25–30° C. Serial sections were prepared through the brains of seventeen snakes as follows:

(i) Two normal brains were fixed in a mixture of 90 c.c. of 50 % alcohol, 5 c.c. of formalin and 3·5 c.c. of glacial acetic acid. A transverse and a horizontal series of sections were cut in paraffin at 12 μ. The former was stained with gallocyanin, and the latter with cresyl violet.

(ii) The brains of fifteen snakes, in which the left optic nerve had been cut, were impregnated in block by Nonidez's (1939) silver method. Of these, nine were cut transversely, two sagittally and four in the horizontal plane, all at 7 μ. Post-operative survival times for the transverse series were 7, 8, 10, 13, 15, 25, 30, 88 and

136 days, for the sagittal series 13 and 22 days, and for the horizontal series 9, 11, 12 and 77 days.

All operations were performed under ether anaesthesia and with aseptic precautions. Care was taken to avoid traction at the optic chiasma. When the optic nerve had been cut a short length of it was removed, with the eye, in order to avoid the possibility of necrosis and infection. The orbital cavity was packed with penicillin-sulphathiazole powder. '*Oxycel*', a gauze type coagulant, was useful in arresting haemorrhage. The animals were ultimately killed by decapitation; the brain was exposed rapidly and fixed *in situ* for 24 hr. before removal.

NORMAL ANATOMY

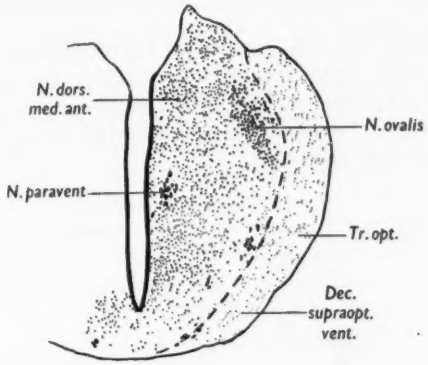
It is necessary to describe briefly the normal appearance of certain parts of the thalamus and midbrain related to the optic pathways. The terminology which is used includes many terms which have appeared frequently in the literature of reptilian neurology. It should be noted that some of these terms have not always been applied by different workers to corresponding structures. The need for caution in assuming homologies, even within the Reptilia, is therefore obvious.

Lateral geniculate nucleus. This nucleus lies in the lateral part of the diencephalon and is found at all levels except the extreme rostral pole. In sections through the middle and caudal parts of the thalamus it is clearly divisible into a lateral neuropil and a medial cell plate (Text-fig. 1*b*). The lateral neuropil is directly medial to the optic tract, and small cells are scattered amongst the fibres. A few larger rounded cells are present in a narrow zone immediately adjacent to the optic tract, where the neuropil is particularly dense. The lateral neuropil extends rostrally to a point just lateral to the caudal part of the nucleus ovalis (Text-fig. 1*a*). The medial cell plate is a broad band of mixed large and small cells. It is convex laterally but separated from the optic tract by the lateral neuropil. The large cells are fusiform or stellate; they send thick processes laterally to ramify within the lateral neuropil. When followed into the rostral part of the thalamus the medial cell plate becomes ill defined. It appears to separate into dorsal and ventral parts, both of which become indistinguishable from the nucleus dorsolateralis anterior. A strong fasciculus geniculatus descendens runs ventro-caudally from the lateral geniculate nucleus into the ventral part of the tegmentum.

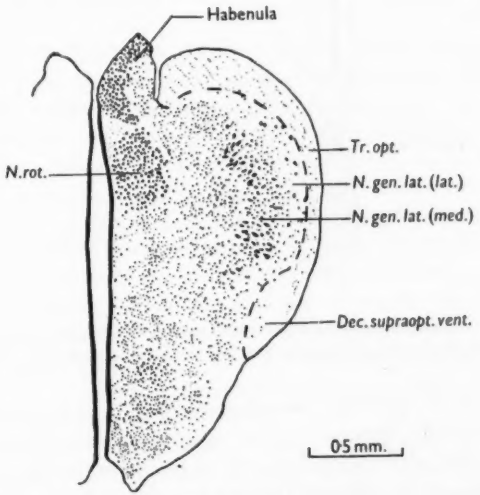
The lateral geniculate nucleus in *Natrix* is fundamentally similar to that of *Lacerta* (Beccari, 1923; Armstrong, 1950) and other reptiles. The main difference lies in the relatively poor differentiation of the medial cell plate in the snake. Illustrations by Warner (1931, 1947) suggest that in this respect the lateral geniculate nucleus in *Crotalus* resembles that of *Natrix*. It is to be noted, however, that Warner himself has followed Frederikse (1931) in applying the term 'corpus geniculatum laterale' only to that part which I have called the lateral neuropil.

Nucleus ovalis. This is a well-defined fusiform cell mass lying obliquely in the lateral part of the rostral pole of the thalamus (Text-fig. 1*a*). The component cells are small and densely packed. Caudally it is replaced by the medial cell plate of the lateral geniculate nucleus. There is no doubt that it corresponds to the nucleus ovalis described in other reptiles (Huber & Crosby, 1926; Cairney, 1926; Papez, 1935; Addens, 1938), and an almost identical formation in *Crotalus* was illustrated by

Warner (1931) in his fig. 12, but labelled as part of the lateral geniculate nucleus. A statement by Kappers (1947) that the nucleus ovalis is poorly developed or absent in snakes appears to be incorrect.



Text-fig. 1*a*.



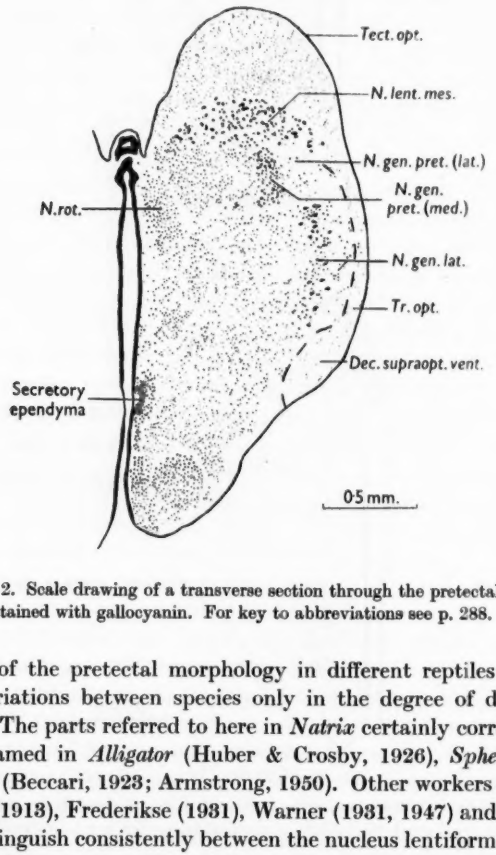
Text-fig. 1*b*.

Text-fig. 1. Scale drawings of transverse sections stained with gallocyanin: (*a*) through the rostral pole of the thalamus; (*b*) through the middle of the thalamus. For key to abbreviations see p. 288.

Pretectal region. The nucleus lentiformis mesencephali and the nucleus geniculatus pretectalis are readily identified (Text-fig. 2). They are similar in form and relations to the structures of the same name which were described in *Lacerta*. Sagittal silver series reveal a well-developed fasciculus geniculatus pretectalis descendens.

The nucleus pretectalis lies directly caudal to the nucleus lentiformis mesencephali, and is traversed by the usual fibre bundles passing between the diencephalon and the deeper layers of the optic tectum. Its caudal margin is well defined, but the boundary between it and the nucleus lentiformis mesencephali is much less distinct than in the lizard.

The nucleus posterodorsalis is a conspicuous feature in *Natrix*. It forms a small prominence medial to the optic tectum and overlying the posterior commissure (Pl. 3, fig. 9). Silver preparations show that it consists mainly of a characteristic neuropil, in which there are rounded areas composed of exceedingly fine fibres. Between these areas are a few small cells.



Text-fig. 2. Scale drawing of a transverse section through the pretectal region stained with gallocyanin. For key to abbreviations see p. 288.

A comparison of the pretectal morphology in different reptiles reveals a basic pattern, with variations between species only in the degree of differentiation of particular nuclei. The parts referred to here in *Natrix* certainly correspond to structures similarly named in *Alligator* (Huber & Crosby, 1926), *Sphenodon* (Cairney, 1926) and *Lacerta* (Beccari, 1923; Armstrong, 1950). Other workers such as Edinger (1899), de Lange (1913), Frederikse (1931), Warner (1931, 1947) and Kappers (1947) have failed to distinguish consistently between the nucleus lentiformis mesencephali, the nucleus geniculatus pretectalis and the nucleus pretectalis, and this is mainly responsible for prevailing confusion in the terminology of the reptilian pretectal region.

The nucleus posterodorsalis is of special interest in view of the considerable variation of its extent in different reptiles. It was first described by Huber & Crosby

(1926, 1933) in *Alligator* and *Anolis*, in which it appears to be moderately developed. In *Lacerta* it is extremely small. The so-called 'area pretectalis' of the Chelonia (Papez, 1935) is almost identical with the nucleus posterodorsalis of *Natrix*.

Optic tectum. Lamination of the tectum in *Natrix* is less elaborate than in *Lacerta*, but the same principal strata can be identified. The stratum zonale is a thin surface layer of neuropil containing few cells, and unlike that of the lizard is of uniform appearance over the whole extent of the tectum. The stratum opticum consists of the usual fibre bundles; but in *Natrix* they form a more sharply defined and uniform layer than in *Lacerta*. The most striking difference between the optic tecta of the snake and the lizard is in the stratum fibrosum et griseum superficiale. That of *Natrix* is relatively thinner, and in silver preparations does not present the division into substrata which is so obvious in the lizard. For further details of normal anatomy reference should be made to the comparative study of the reptilian optic tectum, including that of *Natrix*, by Huber & Crosby (1933).

EXPERIMENTAL RESULTS

Post-operative degeneration of the axons and their terminals was similar to that which occurs in *Lacerta*, although some differences were apparent, especially with regard to the time factor.

Axonal degeneration. Seven days after operation the severed retinal fibres had developed a slightly increased affinity for silver as compared with those from the normal side. After 8 days sporadic swellings were apparent in the degenerating fibres, and the difference in staining quality had become pronounced, making a striking contrast with the normal. In animals surviving between 9 and 12 days the degenerating fibres were identified without difficulty. Masses of fusiform swellings were arranged along them like beads, and in some places the slender segments between the swellings showed signs of rupture (Pl. 1, fig. 3). By 13 days axonal disintegration was advanced, and heavily staining fragments were present throughout the primary visual pathways (Pl. 1, fig. 4). These fragments had almost completely disappeared after 15 days, leaving only a small amount of argentophil debris. The 22- and 30-day series showed similar but rather more advanced stages of resorption. Traces of granular debris were still present after 77 and 88 days, but none at all could be seen in the 136-day specimen.

Terminal degeneration. Terminal degeneration of the bouton type (Hoff, 1932) occurred in various diencephalic and midbrain centres into which the degenerating retinal fibres could be traced. Typical terminal boutons could not be demonstrated in these areas in the normal state, but many fine argentophil ring-like structures were present 7 days after the operation. Between 8 and 12 days they were seen in increasing profusion and showed the intense affinity for silver which is a characteristic of degenerating terminals. The majority became enlarged and greatly thickened (Pl. 2, fig. 7), and in some cases solid terminal bulbs developed by total obliteration of the central lumen. It was clear, however, that all of the boutons did not undergo an identical sequence of changes. Many had attained a large size after only 8 days, others developed into solid bulbs without conspicuous enlargement, and

yet others remained both small and annular throughout. After 13 days the total number of rings and bulbs had diminished appreciably, and by 15 days all but a few had disappeared. Degeneration of the nerve terminals was associated with the usual swelling, vacuolation and ultimate fragmentation of the terminal arborizations of the retinal fibres. This resulted in a striking lack of neuropil in the primary visual centres from the 15th day onwards.

The material prepared in this investigation indicated a fairly constant time sequence for degeneration under the conditions in which the animals were kept, and only one specimen showed variation in this respect. This animal was killed 25 days after section of the optic nerve; it showed degenerative changes more typical of about 12 days.

The Visual Pathways

(i) *Optic nerve and chiasma.* The normal optic nerve in *Natrix* is divided by fine connective tissue septa into a large number of separate fascicles. The nerve fibres in each fascicle are disposed around a central column of cells which have large, vesicular nuclei and scant cytoplasm (Pl. 1, fig. 1); they are evidently glial elements, but their significance is uncertain. In longitudinal sections it seems that at least some of the cell columns are continuous from the eyeball to the optic chiasma. In the chiasma fasciculation of the optic nerve is lost and the cells become less numerous and segregated into short rows. The optic nerve as a whole divides into bundles, usually of very unequal size, which interlock with those from the opposite side. There is individual variation in the number, size and disposition of these bundles, but a frequent arrangement is for one nerve to form three bundles and the other nerve two. Section of the optic nerve resulted in degeneration of nearly all fibres in the central stump of the nerve. Decussation at the chiasma was almost complete, but a small proportion of the degenerating fibres remained uncrossed. The uncrossed element consisted of two groups of fibres, one of which passed on to the rostral surface of the homolateral optic tract, while the other turned sharply on to its ventral surface. The partial nature of the decussation was particularly obvious in the experiments of long duration, where the normal uncrossed component could easily be followed into the degenerated optic tract (Pl. 3, fig. 10).

After resorption of axonal debris, i.e. in the 77-, 88- and 136-day specimens, a few nerve fibres of normal appearance were still present in the central stump of the divided optic nerve (Pl. 3, fig. 11). The persisting fibres were scattered throughout the nerve, but were slightly more numerous dorsomedially than elsewhere.

Dorsal and ventral supraoptic (post-optic) decussations are closely related topographically to the optic chiasma. As the present experiments are not directly concerned with these systems it is sufficient to note that in *Natrix* they are essentially similar to those described in *Lacerta* (Armstrong, 1950).

(ii) *Optic tracts.* On emerging from the chiasma the optic tracts pass dorsolaterally on the surface of the hypothalamus. Section of the left optic nerve was followed, of course, by massive axonal necrosis in the contralateral tract. Degenerating fibres on the inner aspect of the tract were very intimately related to the adjacent hypothalamus. Some of them ran for short distances through the suprachiasmatic nucleus, and then rejoined the optic tract. Others, more laterally situated, entered the supraoptic

nucleus; here they intermingled in a plexiform manner with the outermost of the large neurosecretory cells which occur in this nucleus. However, it was clear on examination of serial sections that at least the majority of these fibres, and probably all of them, also passed back into the optic tract. No evidence of terminal degeneration could be found in the supraoptic nucleus, nor in any other part of the hypothalamus.

The basal optic root, or 'posterior accessory optic tract' is represented by coarse fibres which part from the optic tract as it approaches the level of the lateral forebrain bundle. They pass superficial to the pars ventralis of the ventral supraoptic decussation, and form a band-like tract which runs caudally to reach the nucleus opticus tegmenti. Division of the left optic nerve resulted in degeneration of the contralateral basal optic root. Degenerating terminals appeared in the nucleus opticus tegmenti in relation to the cell bodies and their dendrites (Pl. 2, fig. 6). Disappearance of the retinal fibres showed that the basal optic root is joined by a small number of fibres from the pars ventralis of the ventral supraoptic decussation. These, of course, did not degenerate. They are of two kinds: those which enter the nucleus opticus tegmenti with the retinal fibres, and others which sink into the lateral part of the hypothalamus and seem to constitute an interhypothalamic component of the ventral supraoptic decussation.

The main optic tract passes round the lateral forebrain bundle and runs dorsocaudally on the lateral surface of the thalamus. After section of the left optic nerve numerous degenerating fibres could be seen turning medially from the optic tract into the opposite lateral geniculate nucleus. These appeared to be both stem fibres and collaterals, but the distinction is by no means easy to make, even in serial sections. Profuse terminal degeneration occurred throughout the lateral neuropil (Pl. 2, fig. 5), degenerating boutons being specially numerous close to the optic tract. Fewer terminal rings and bulbs were encountered in direct relation to the cell bodies of the medial cell plate. This suggests that the synaptic relationship between the retinal fibres and the lateral geniculate nucleus is, as in *Lacerta*, predominantly axo-dendritic.

A few bundles of retinal fibres leave the optic tract dorsal to the lateral forebrain bundle, and pursue a separate course dorsocaudally through the lateral part of the thalamus. These represent the axillary optic tract of Huber & Crosby (1933). They are accompanied by fibres from the pars dorsalis of the ventral supraoptic decussation, from which they are indistinguishable in the normal state. Some of the more rostral axillary tract fibres pass through the nucleus ovalis, but no evidence of terminal degeneration could be found there. Many of these fibres terminate in the lateral neuropil of the lateral geniculate nucleus; others rejoin the main optic tract on its inner surface, but some continue independently into the lateral part of the pretectal region and the optic tectum.

A large number of crossed retinal fibres terminate in the pretectal region. Degenerating stem fibres and collaterals were traced medially from the main optic tract into the nucleus geniculatus pretectalis and the nucleus lentiformis mesencephali. These fibres form part of the so-called 'brachium tecti medialis' (Huber & Crosby, 1933). Degenerating terminals were very numerous throughout the lateral neuropil of the nucleus geniculatus pretectalis, and rather less so in the

nucleus lentiformis mesencephali. No evidence was found of retinal connexions with the nucleus pretectalis. Medial to the optic tectum a small and separate bundle of degenerating fibres could be traced from the optic tract into the nucleus posterodorsalis. This nucleus was also seen to be reached by a few degenerating fibres which passed through the nucleus lentiformis mesencephali in the brachium tecti medialis. The characteristic neuropil of the nucleus posterodorsalis was observed to fragment and finally to disappear almost completely after division of the opposite optic nerve (Pl. 3, fig. 9).

In *Natrix*, as in the lizard, the majority of the crossed retinal fibres ultimately enter the stratum opticum of the optic tectum. Only a small number of fibres persist in this layer of the tectum when the opposite optic nerve has been cut (Pl. 3, fig. 9). Small bundles of degenerating fibres from the main and axillary optic tracts could also be followed directly into the stratum fibrosum et griseum superficiale. From the stratum opticum many of the fibres were traced into the stratum zonale, but the majority turned abruptly from the stratum opticum into the underlying stratum fibrosum et griseum superficiale.

Terminal degeneration was extensive throughout the stratum fibrosum et griseum superficiale (Pl. 2, fig. 7), but was also seen over the whole surface of the tectum in the stratum zonale (Pl. 2, fig. 8). No evidence was found for the termination of retinal fibres in deeper layers; nor were any degenerating fibres seen to cross the midline in the tectum.

(iii) *Uncrossed retinal fibres.* The position of the uncrossed fibres at the chiasma has already been described. Their subsequent course was revealed equally well by two alternative methods of study; either by tracing axonal degeneration in the homolateral optic tract, or by following the normal uncrossed fibres in the contralateral tract after resorption of the crossed retinal fibres.

It was found that the uncrossed fibres at first remain superficial, on the rostral and ventral surfaces of the optic tract. Soon they swing over to the inner aspect of the tract, and converge to form a small, compact bundle. This could be followed round the lateral forebrain bundle into the neuropil which forms the rostral extremity of the lateral geniculate nucleus. A small amount of terminal degeneration was consistently located in this part of the homolateral geniculate nucleus.

Uncrossed fibres could not be traced into any other part of the lateral geniculate nucleus, nor to any of the other visual centres.

(iv) *Non-retinal components of the optic tract.* After degeneration and resorption of the crossed retinal fibres there remained a considerable number of normal fibres in the optic tract, quite apart from the uncrossed retinal component. Reference has already been made to the small proportion of optic nerve fibres which were unaffected by the operation. In the long duration experimental series these persisting fibres were traced without difficulty through the optic chiasma into the contralateral optic tract. A few of them, in the deeper part of the tract, appeared to enter the suprachiasmatic and supraoptic nuclei of the hypothalamus and could be traced no further; the majority, however, continued round the lateral forebrain bundle in the optic tract. Beyond this point it was impossible to distinguish them among the numerous non-retinal fibres which enter the optic tract at thalamic and pretectal levels.

The remaining non-retinal components may, for descriptive purposes, be divided into two groups, both of which join the optic tract on the lateral surface of the thalamus and in the pretectal region. These experiments do not, of course, indicate either the origin or the termination of these fibres. First, there is a contribution from the pars dorsalis of the ventral supraoptic decussation. Bundles of these fibres sweep into the lateral part of the thalamus in company with the axillary optic tract. Some of them incline laterally, and enter the main optic tract on its inner aspect. The second group consists of a large number of fibres which enter the optic tract from the lateral geniculate nucleus, the nucleus geniculatus pretectalis and the nucleus lentiformis mesencephali. They turn sharply dorsalwards and pass with the supraoptic fibres into the stratum opticum and the stratum fibrosum et griseum superficiale of the optic tectum.

DISCUSSION

Existing knowledge of the characteristics of axonal and terminal degeneration in the central nervous system of submammalian vertebrates is very limited. Experiments on the visual pathways of *Lacerta vivipara* revealed a succession of degenerative changes morphologically similar to those which are now well known in mammals, but they occurred much more slowly. It was observed, too, that the rate of degeneration in the poikilothermic lizard is controlled by the temperature of the environment. The present work on *Natrix* has now shown that the degenerative process in the snake is in certain respects different both from that of mammals and from that described in the lizard. In snakes kept at 25–30° C. the onset of visible degeneration in the severed axons and at the nerve endings is about as slow as in the lizard. Subsequent disintegration and resorption, however, are considerably more rapid; thus, more axonal debris remained in the optic nerve of *Lacerta* 11 weeks after the operation than was found in *Natrix* after only 22 days. Another feature of axonal degeneration in *Natrix* was the abundance of fusiform, bead-like swellings which developed between 9 and 12 days after the operation. Swellings are, of course, a common feature of axonal degeneration in mammals, and they were also seen in the lizard; but the regular occurrence of a stage when they predominate, almost to the exclusion of other forms of axonal distortion, appears to be unusual.

On the basis of these observations in reptiles it seems probable that appreciable variation in the characteristics of degeneration in different species, and possibly in different parts of the brain in the same species, may be encountered in future experimental studies on cold-blooded vertebrates.

With the aid of experimental data it is now possible to compare certain aspects of the organization of the visual system in *Natrix* and *Lacerta*. Attention has been drawn to the remarkable fasciculation of the optic nerve in the snake, and to the long rows of cells which it contains. In these features, however, it does not seem to differ fundamentally from the optic nerve of *Lacerta* or from those of other reptiles (Gross, 1903); the difference is only one of degree. The optic chiasma in *Natrix* contains fewer and, for the most part, larger decussating bundles than in *Lacerta*. This is in keeping with the very wide range of chiasma morphology which was shown by Gross to be a peculiarity of the Reptilia.

Perhaps the most striking feature of the present experimental results is the fact that they demonstrate such a close resemblance between the central optic pathways and the primary visual centres of the snake and those of the lizard. The crossed retinal fibres have an almost identical course and terminal distribution in the two animals. The only exception to this is the presence in *Natrix* of optic connexions with a well-differentiated nucleus posterodorsalis in the pretectal region. No such connexion could be found in *Lacerta*, where the nucleus posterodorsalis was found to be very poorly developed. This does not constitute an essential difference between snakes and lizards, for Huber & Crosby (1933) described a connexion between the optic tract and a fairly well-developed nucleus posterodorsalis in the American lizard, *Anolis*. The fascicle concerned was designated 'S' by Huber & Crosby, and assumed to be of retinal origin.

In both *Natrix* and *Lacerta* the experimental method has failed to demonstrate a direct retino-hypothalamic pathway, and there is certainly nothing comparable with the massive hypothalamic optic root stated by Frey (1937, 1938) to be present in certain mammals and amphibians. Other workers (e.g. Jefferson, 1940; Herrick, 1948) have already questioned the validity of Frey's interpretation. Similarly, no evidence has been found in the reptiles studied that any retinal fibres terminate in the nucleus ovalis. Certain axillary optic tract fibres were seen to pass through this nucleus; it therefore seems possible that optic fibres described in normal preparations of this region (e.g. by Papez, 1935, in turtles) may also have been fibres of passage. Cairney (1926), Papez (1935) and Addens (1938) believe that the reptilian nucleus ovalis may be homologous with the nucleus of Bellonci in amphibians. This hypothesis is called into question by the absence of optic connexions with the nucleus ovalis. On the other hand, it still remains to be proved experimentally that such a connexion does in fact exist with the amphibian nucleus of Bellonci as is commonly believed.

The uncrossed optic pathway in *Natrix* is very similar to that of *Lacerta*, but it was possible to trace these fibres with rather more ease and precision in the present experiments than in those on the lizard. Some evidence was obtained in *Lacerta* that uncrossed fibres may terminate in the lateral neuropil at the rostral extremity of the lateral geniculate nucleus; it is now clear that most and perhaps all of the uncrossed fibres in *Natrix* terminate in a corresponding area of the geniculate nucleus. In both snake and lizard this part of the lateral geniculate nucleus also receives crossed retinal fibres. It is just possible that a few of the uncrossed fibres continue dorsocaudally in the optic tract, becoming obscured in the available material by the numerous non-retinal fibres which enter the tract as it runs over the surface of the thalamus. It should be noted, however, that no terminal degeneration could be found in the homolateral pretectal region or optic tectum of either *Natrix* or *Lacerta*.

An interesting finding in *Natrix* is the presence of a number of fibres in the optic nerve which showed no sign of degeneration as much as 19 weeks after the operation. All trace of degenerating nerve fibres had vanished by that time; it is therefore scarcely possible that the remaining fibres of normal appearance were merely slow to degenerate. The possibility of incomplete division of the optic nerve can be dismissed, for a short length of the nerve was always removed. Thus, it may reasonably be assumed that the persisting fibres were not of retinal origin. Careful

search revealed no aberrant ganglion cells or other neurones from which the fibres might arise in the optic nerve. It is therefore concluded that these fibres constitute an efferent or centrifugal component of the nerve. The experiments showed clearly that all of them cross in the chiasma from the contralateral optic tract, and no evidence was found of an inter-retinal connexion. The precise origin of the efferent fibres remains unknown; it is possible, but by no means certain, that a few of them enter the optic tract from the suprachiasmatic and supraoptic nuclei of the hypothalamus.

Existing anatomical evidence of efferent optic nerve fibres in vertebrates is fragmentary, and to a large extent contradictory. According to Kappers, Huber & Crosby (1936) they have been reported in certain fishes, birds and mammals, but apparently not in reptiles. Many of these reports were based on the examination of normal material; as such they are of doubtful significance owing to the relatively small number of the fibres concerned, and to the virtual impossibility of determining from normal preparations the direction in which impulses are conducted. Ramon y Cajal (1911), in the course of detailed studies on the retina of birds and mammals, described the terminal arborization of certain fibres in relation to the amacrine cells. He believed these to be centrifugal optic nerve fibres, but was uncertain of their origin. Most of the experimental evidence so far advanced is also inconclusive; but the experiments of Wallenberg (1898) and of Kosaka & Hiraiwa (1915) provide convincing evidence that the tractus isthmo-opticus in birds is indeed a centrifugal pathway. In certain marsupials, on the other hand, more recent work in which silver impregnation was used (Bodian, 1937; Packer, 1941) failed to reveal any persisting optic nerve fibres after removal of an eye. It is clear that a comprehensive investigation of this problem, using modern experimental techniques and including representatives of all the vertebrate classes, will be necessary to elucidate the true state of affairs.

At present one can only speculate on the functional significance of the efferent fibres which are evidently present in *Natrix*. It is conceivable that they play some part in the control of pupillary reflexes. Alternatively, they may serve as a pathway for the control of photomechanical changes in the pigment epithelium and photoreceptors of the retina (Engelmann, 1885). The latter hypothesis gains support from physiological evidence that efferent optic nerve fibres participate in retinal photomechanical changes in *Ameiurus* (Arey, 1916). In other fishes and the frog, however, the retinal changes do not depend on the integrity of the optic nerve. Moreover, there is some doubt about the actual occurrence of photomechanical changes in reptiles (Walls, 1942). It may be, therefore, that the centrifugal fibres are involved in some other retinal mechanism as originally postulated by Ramon y Cajal; possibly their role is to modify, by facilitation or inhibition, the passage through the retina of centripetal impulses originating from the photoreceptors.

It is noteworthy that in *Lacerta* no persisting fibres could be found in the optic nerve after it had been cut (Armstrong, 1950), and this may indicate an essential difference between the snake and the lizard. However, the longest post-operative survival time for *Lacerta* was 11 weeks, and in the lizard a good deal of axonal debris still remained at that time. The debris may have obscured a small number of persisting fibres, and this point merits further investigation.

We may now consider the results of the present investigation in relation to the theory of the evolution of Ophidia from burrowing lizards (Walls, 1942). This theory is based primarily upon the existence of certain fundamental differences, anatomical, embryological and physiological, between the eyes of snakes and those of other vertebrates. One might imagine that such a radical reconstruction of the peripheral visual organ as that indicated by Walls would be reflected in the organization of the central visual apparatus. The primary visual centres in *Natrix* are on the whole less clearly differentiated than in *Lacerta* and many other reptiles; but they conform to a generalized reptilian pattern. Relatively poor differentiation is, in fact, characteristic of many of the cell masses in the forebrain and midbrain of snakes, and is not restricted to the visual centres. With regard to the visual pathways, it is true that certain differences were noted between *Natrix* and *Lacerta*. But it is evident from the foregoing discussion that fasciculation of the optic nerve, the presence of optic connexions with the nucleus posterodorsalis, and the existence of centrifugal optic nerve fibres are not exclusively ophidian characteristics. In brief, the results of this investigation provide no definite evidence in support of the theory advanced by Walls.

SUMMARY

1. Diencephalic and midbrain centres related to the optic tract system in *Natrix* have been described and compared with corresponding structures in other reptiles.

2. The brains of fifteen snakes were impregnated with silver at intervals up to 136 days following section of an optic nerve. Serial sections were examined for axonal and terminal degeneration. Degenerative changes were quite similar to those previously described in the lizard, but resorption of axonal debris occurred much more rapidly in the snake.

3. Experimental evidence was obtained for the following conclusions:

(*a*) The optic nerve consists mainly of fibres of retinal origin, but also contains a small number of efferent fibres.

(*b*) Most of the retinal fibres decussate at the optic chiasma, but a small proportion remain uncrossed.

(*c*) Crossed retinal fibres pass in the main and axillary optic tracts to terminate in the lateral geniculate nucleus, the nucleus geniculatus pretectalis, the nucleus lentiformis mesencephali, the nucleus posterodorsalis and the optic tectum; others pass in the basal optic root to the nucleus opticus tegmenti. There is no direct retino-hypothalamic connexion.

(*d*) Uncrossed retinal fibres run in the main optic tract and terminate in the rostral extremity of the lateral geniculate nucleus.

4. There is a close resemblance between the primary visual pathways of *Natrix* and those of *Lacerta*. They provide no evidence of a reconstruction of the ophidian visual system in phylogeny.

5. The problem of efferent optic nerve fibres and their functional significance has been reviewed and discussed in the light of the present experimental findings.

My thanks are due to Prof. F. Goldby for his advice and encouragement throughout the course of this work.

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EXPLANATION OF PLATES

Plate 1

Fig. 1. Longitudinal section through a normal optic nerve stained with cresyl violet. Columns of glial cells are seen in the centre of the nerve fascicles. (×270.)

Fig. 2. The normal appearance of fibres in the optic tract. Nonidez's method. (×1100.)

Fig. 3. Axonal degeneration in the right optic tract 10 days after section of the left optic nerve. Fusiform axonal swellings are present, and some fibres have ruptured between the swellings. Nonidez's method. (×1100.)

Fig. 4. Axonal disintegration in the right optic tract 13 days after section of the left optic nerve. Nonidez's method. (×1100.)

Plate 2

Fig. 5. Degenerating terminals and fibres in the lateral neuropil of the lateral geniculate nucleus 13 days after division of the opposite optic nerve. Nonidez's method. (×1600.)

Fig. 6. Terminal degeneration in the nucleus opticus tegmenti 11 days after division of the opposite optic nerve. Nonidez's method. (×1600.)

Fig. 7. An enlarged, thickened and strongly argentophil terminal bouton in the stratum fibrosum et griseum superficiale of the optic tectum. Opposite optic nerve cut 10 days previously. Nonidez's method. (×1600.)

Fig. 8. Degenerating terminals and fibres in the stratum zonale at the caudal extremity of the optic tectum. Opposite optic nerve cut 8 days previously. Nonidez's method. (×1600.)

Plate 3

Fig. 9. Transverse section through the region of the posterior commissure 136 days after division of the left optic nerve. Extensive degeneration has occurred in the contralateral optic tectum, and is most obvious in the stratum opticum. Note also the disappearance of neuropil from the contralateral nucleus posterodorsalis. Nonidez's method. (×105.)

Fig. 10. Transverse section through the optic chiasma 136 days after section of the left optic nerve. A fascicle of uncrossed fibres is shown turning from the right (normal) optic nerve on to the ventral surface of the degenerated homolateral optic tract. Nonidez's method. (×420.)

Fig. 11. Longitudinal section through the central stump of the left optic nerve 77 days after it had been divided. Several persisting fibres of normal appearance are present; such fibres were seen throughout the nerve. Nonidez's method. (×540.)

List of Abbreviations

Dec. supraopt. vent.	Decussatio supraoptica ventralis
N. dors. med. ant.	Nucleus dorsomedialis anterior
N. gen. lat.	Nucleus geniculatus lateralis
N. gen. lat. (*lat.*)	Nucleus geniculatus lateralis (lateral neuropil)
N. gen. lat. (*med.*)	Nucleus geniculatus lateralis (medial cell plate)
N. gen. pret. (*lat.*)	Nucleus geniculatus pretectalis (lateral neuropil)
N. gen. pret. (*med.*)	Nucleus geniculatus pretectalis (medial cell plate)
N. lent. mes.	Nucleus lentiformis mesencephali
N. ovalis	Nucleus ovalis
N. paravent.	Nucleus paraventricularis
N. rot.	Nucleus rotundus
Tect. opt.	Tectum opticum
Tr. opt.	Tractus opticus

Fig. 1.

Fig. 2.

Fig 3.

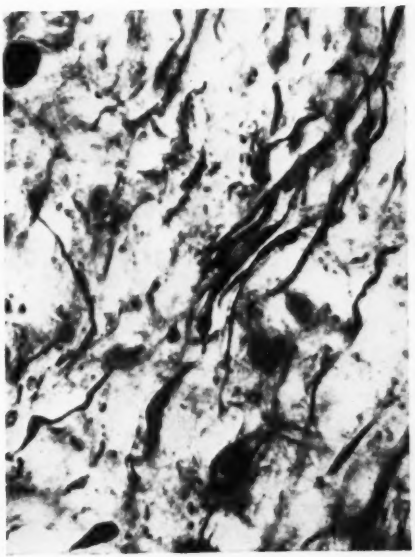

Fig. 4.

Fig. 5.

Fig. 6.

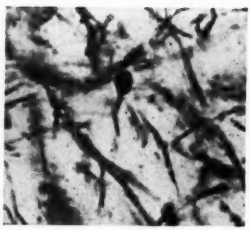

Fig. 7.

Fig. 8.

ARMSTRONG—THE VISUAL PATHWAYS IN A SNAKE

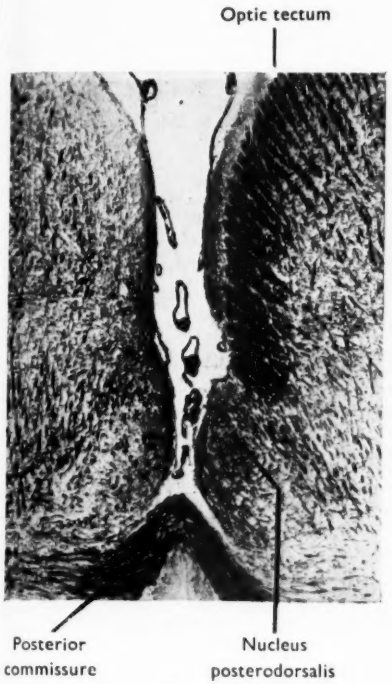

Fig. 9.

Fig. 10.

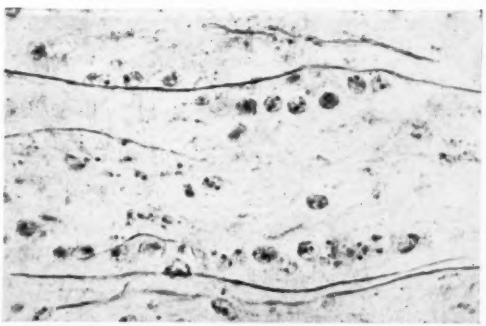

Fig. 11.

ANATOMICAL NOTE

A JUVENILE SKULL EXHIBITING DUPLICATION OF THE OPTIC CANALS AND SUBDIVISION OF THE SUPERIOR ORBITAL FISSURE

By R. Warwick, *Department of Anatomy, University of Manchester*

Soemmerring (1794) and Theile (1843) drew attention to the rarity of duplication of the optic canal, without, however, recording particular examples. Both stated that the inferior and smaller canal had been observed to transmit the ophthalmic artery, a finding supported by Dubreuil (1843). Henle (1871) mentioned the condition, and Visconti (1885) and Zoja (1885, 1886) recorded details of two and five instances respectively. Calori (1891) refers to two cases, both unilateral. Le Double (1903) described a further case. White (1924) saw the anomaly thrice in 164 skulls, and Keyes (1935) noted five examples in 2187 skulls, thirty-six of which displayed a groove, rather than a foramen, in the floor of the optic canal. Augier (1931) reported that cases had also been seen by Adachi, Calori and Taguchi. Whitnall (1932) showed a photograph of the condition.

This rare anomaly has been seen in both sexes, at various ages, and in a number of races. Adequate details are lacking in many reports, but bilateral cases appear to be unusual. Apart from the present subject, bilateral canals have been recorded thrice only—by Visconti (1885), Zoja (1885), and le Double (1903).

The skull whose peculiarities have been reported below formed part of the remains of a boy aged 21 months, whose body had been the subject of forensic examination. In the course of clearing away the remaining soft tissues bilateral duplication of the optic canal was discovered (Pl. 1, figs. 1 and 2). The disturbance caused by post-mortem examination and decomposition excluded absolute certainty of the contents of all the canals, since the remains were not examined anatomically until over 3 weeks after the death of the child. But the superior and larger openings were occupied by a large nerve and dura mater, doubtless the optic nerve, while the lower right canal contained an artery of the size customary in the ophthalmic.

The superior canals were almost triangular in shape (Pl. 1, fig. 1). The greatest diameter of the right one was 5·5 mm., that of the left 6 mm.; the least diameter of both was 4 mm. The length of the canals was not less than 5 mm., but accurate measurement was impossible, owing to the imperceptible expansion of their anterior orifices into the orbital walls. Few records of the dimensions of the optic canal in very young children appear to exist, but White (1924) stated that it was oval or round and never less than 4·5 mm. in diameter in twenty newborn infants.

The smaller foramina, which were presumed to have contained the ophthalmic arteries, lay in the lesser wing of the sphenoid immediately inferior to the true optic canals (Pl. 1, figs. 1 and 2). They were both transversely oval, approximately 2 mm. in diameter, and were separated from the optic canals above by a thin plate of bone, measuring 5 mm. along the axis of the canals and of a maximum thickness slightly less than 1 mm. These accessory optic, or ophthalmic canals were directed posteriorly and medially towards the sulci for the carotid arteries at the anterior extremity of the cavernous sinus. They lay entirely in the inferior root of the lesser wing, the metopic bar of some authorities.

Calori (1891) and le Double (1903) have both ascribed this anomaly to ossification of the process of dura mater between the optic nerve and ophthalmic artery. This view accords with the observation that the artery usually occupies the inferior canal. Since, however, ossification of structures which normally consist of soft tissues is regarded as characteristic of the later decades of life, the age incidence of the anomaly is of some interest. The following are the few records available:

Visconti (1885): 1 adult male, right side only; 1 hydrocephalic infant, bilateral.

Zoja (1885, 1886): 1 female, 18 years, right side only; 1 male, 35 years, right side only; 1 male, 20 years, right side only; 1 male, 'aged', left side only; 1 female, 30 years, bilateral.

Le Double (1903): 1 male, 42 years, bilateral.

Present Report: 1 male, 21 months, bilateral.

It will be noted that most of the cases occurred in the earlier decades, and two within the first 2 years of life.

Augier (1931) has suggested that duplicity of the optic canal represents persistence of a foramen, *le trou métoptique*, which he had frequently encountered in foetal skulls. He regarded this foramen as being due to the presence of an aberrant ophthalmic vein.

A further peculiarity in the skull described here lends some support to the views of Calori and le Double rather than to Augier's suggestion. At the inferior end of the left superior orbital fissure a thin sliver of bone bridges the fissure, thus creating a small crescentic foramen at its lower margin and above the foramen rotundum (Pl. 1, figs. 2 and 3). A shallow groove leads back from the foramen towards the site of the cavernous sinus, suggesting that it might have transmitted an inferior ophthalmic vein. The only reference traced in the literature with regard to this anomaly was a figure in a paper by Calori (1891) which portrays a similar foramen, also on the left. The bar of bone separating it from the inferior orbital fissure appears, however, to have been much more substantial. This foramen cannot be regarded as the lateral cranio-pharyngeal canal of Sternberg (1890), which Cruveilhier (1843) also described, since canals of this nature were also present on both sides of the present specimen. It may be noted that the bridge of bone delimiting the foramen from the fissure corresponds with the position accorded to the posterior extension of the orbitalis muscle by Whitnall (1932). Whatever may have been the precursor of the bridge, it does present the appearance of an ossified band or stratum of connective tissue. In this regard it is of interest to note that in the case of two reduplicated optic canals photographed by Whitnall (1932) and Keyes (1935), the bar of bone between the canals is in both cases very thin, resembling the bridge referred to above, while the bar between the double optic canals in the present case is much more substantial (Pl. 1, fig. 1) and does not suggest ossification in a layer of dura mater. Perhaps reduplication of the optic canal may arise from different causes; the material available for comparison is, however, at present too scanty to permit any conclusions.

The skull presented other peculiarities of ossification. Although the anterior fontanelle was still not quite obliterated, the metopic suture had almost completely disappeared (Pl. 1, fig. 5)—an unusually early obliteration. The lambdoid suture contained eleven sutural bones, and at the apices of the lesser wings of the sphenoid were two symmetrical ossicles (Pl. 1, fig. 3); these latter correspond with the os alisphéno-frontale of Augier (1931), which he regards as a sutural bone. Otherwise, the state of ossification, when compared with the sparse information in the literature, appeared to be within the usual limits. The skull as a whole was markedly brachycephalic (C.I. 87·9%) and asymmetrical. The capacity was 1320 c.c.

I am indebted to Dr T. H. Blench for permission to record these observations.

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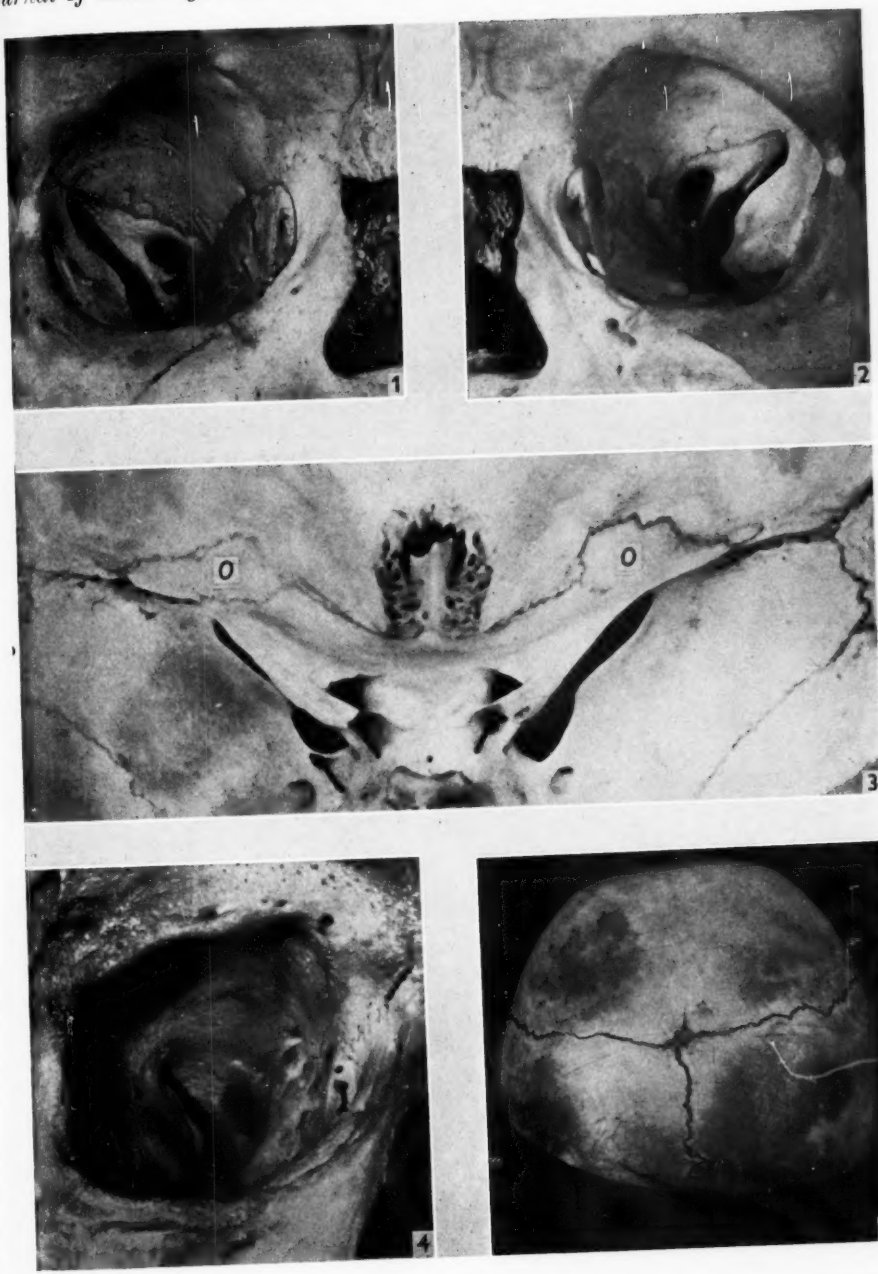

WARWICK—A JUVENILE SKULL EXHIBITING DUPLICATION OF THE OPTIC CANALS AND SUBDIVISION OF THE SUPERIOR ORBITAL FISSURE

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EXPLANATION OF PLATE

Fig. 1. View towards apex of right orbit. Note large triangular optic canal medial to the superior orbital fissure. Below this, in the broad inferior root of the lesser wing, is an accessory optic foramen.

Fig. 2. View towards apex of left orbit. Note duplication of optic canal. At the inferior end of the superior orbital fissure a thin bridge of bone cuts off a crescentic foramen from the fissure. Below this accessory foramen is the foramen rotundum.

Fig. 3. Part of the base of the skull seen from above. Note crescentic accessory foramen, containing a bristle at the lower end of the left superior orbital fissure. The posterior openings of all four optic canals are also visible; the bristles lie in the inferior (accessory) optic canals. At the apices of the lesser wings two ossicles are present (*O,O*).

Fig. 4. Similar view into a normal adult orbit. Compare the inferior root of the lesser wing with that in fig. 1. Note greater depth of the root in the latter.

Fig. 5. Cranium in the region of the bregma viewed from above. Note that the anterior fontanelle is not quite fully ossified, whereas the metopic suture has almost disappeared.

IN MEMORIAM

G. D. CHANNELL, M.B., M.R.C.S.

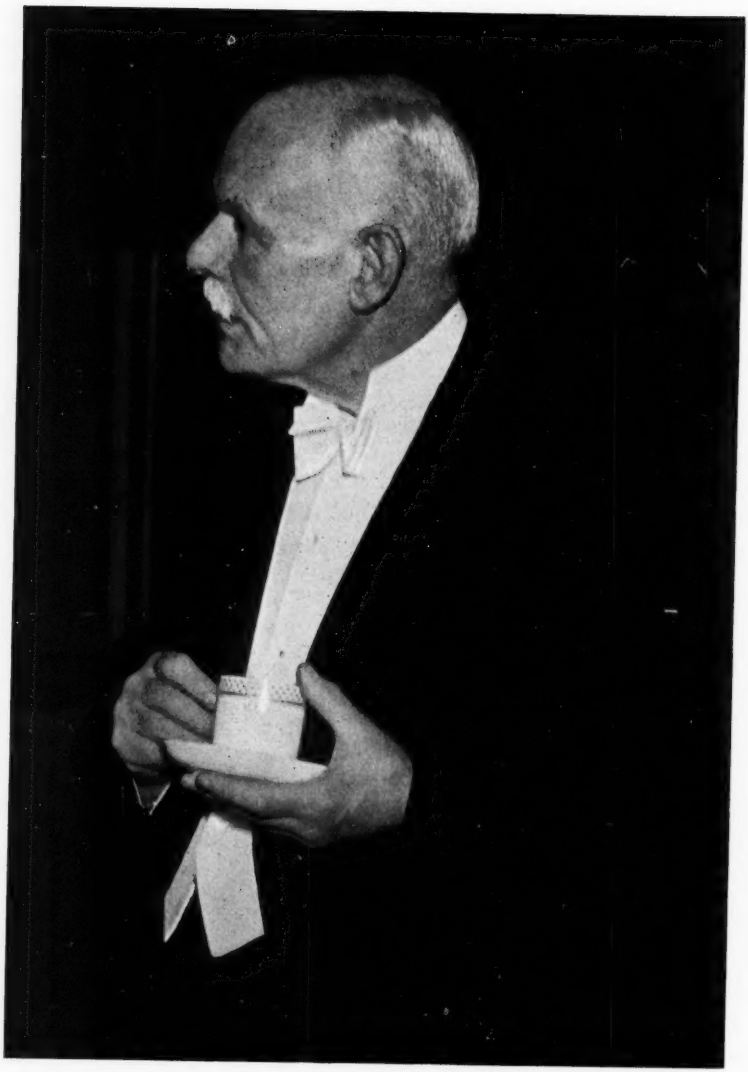
Gerald D. Channell died in tragic circumstances in an explosion at the Brompton Hospital on 27 May 1950.

He was born in Natal in 1911 and came to Guy's in 1931. He won the Hilton prize for dissection in 1933 and, even before qualifying, showed his interest in teaching for he held a succession of student demonstratorships in his school. After qualifying in 1936 he held house appointments at Guy's and then went to the Anatomy department at Cambridge as a demonstrator. His war service was in the navy and during this period he published work on 'immersion foot'.

On returning from war service in 1946 Channell was for three years a junior lecturer in the Anatomy department at Guy's, but he had by then decided that he wished to become a thoracic surgeon. In pursuit of this ambition he obtained his Fellowship diploma and did not hesitate, at considerable financial sacrifice, to take comparatively junior hospital appointments to gain his experience. At the time of his death he had surmounted all his initial difficulties and was holding an appointment as Registrar at the Brompton Hospital. At Guy's he had published, with others, papers on the lumbrical and interosseous muscles and he had become interested in congenital deformities of the heart. It was because he was continuing the latter work in his limited spare time that he happened to be in the Brompton at the time of the explosion which caused his death.

Channell will be remembered especially for his cheerfulness and ready wit and for his capacity for hard, conscientious work. The sympathy of his many friends will go to his widow and child in their tragic loss.

J.W.



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PROFESSOR ALEXANDER LOW

IN MEMORIAM

ALEXANDER LOW, M.A., M.D., LL.D.

By the death of Emeritus Regius Professor Alexander Low on 15 November 1950 in his eighty-third year, the students of Aberdeen have lost one of their finest friends.

The farm of his birth and boyhood on the banks of the River Don lies within sight of the farms where Sir David Ferrier and Sir Arthur Keith were born.

His sixty-four years association with the University began with his study of Arts in 1886. He had a brilliant career in Medicine, graduating in 1894. He was awarded the M.D. Degree, with highest honours, in 1912, and the LL.D. (*honoris causa*) in 1939. In 1894 he was appointed Assistant in Anatomy and was duly promoted Lecturer, Reader and, finally, Professor in 1925. He retired in 1938. He represented the University on the Board of the Rowett Institute for Research in Animal Nutrition, and also the Strathcona Club associated with the Rowett Research Institute. He was a past President of the Anatomical Society of Great Britain and Ireland, and of the Aberdeen Medico-Chirurgical Society, a Director of the Aberdeen Royal Infirmary, a Governor of the Royal Mental Hospital and a member of the Scottish Universities Board. As Dean of the Medical Faculty he welded the union of clinical Professorships in the University with ward appointments in the Hospital—diverse authorities that did not always see eye to eye—a delicate task which partisans of both sides willingly entrusted to his earnest sincerity.

His work upon the development of the lower jaw, to quote the late Prof. Barclay-Smith 'is not only of a high order but has become classical', while Sir Arthur Keith has said 'all his research work has stood the test of time, all of it done with great care, fine judgement and perfect finish'. His histological technique was exquisite, both throughout the process and in its results. The care, precision and detail with which he conducted his investigations upon the burials of the Short Stone Cist or Beaker People, both at the site of discovery and in the laboratory, was a lesson even for the connoisseur. It was amusing to see him quickly and unobtrusively remove a skull from unskilled hands. Disappointed that some teeth had been removed as a memento from a Short Stone Cist skull, he would casually remark that these were very unlucky possessions, and frequently the missing molars would be sure to turn up. It is no wonder that his University possesses the finest collection of the skeletal remains of the Short Stone Cist or Beaker People, for he became galvanized at the news of another 'find'. When aerial flight first started to the Orkneys many years ago, he learned that a rival in Glasgow was on the warpath, and went off post haste and was back in a few hours with a fine skull—one of his students remarked 'up-to-date lad'. He delighted to show a skull recovered from the North Sea in a trawl net, which would be claimed by the expert as a perfect specimen of the Bronze Age, but for one tooth with a dental filling!

As a Physical Anthropologist at a meeting in Oslo some fifteen years ago, he was being teased by Cultural Anthropologists that he could come to no definite decision upon the racial origins of his companions. 'What can you tell us', they said, 'of the

ancestry of the young woman who is conducting our bus tour at the moment'? 'Well,' said Prof. Low, 'one of her parents might be Norse and the other an Aberdonian.' There was no answer to the derision evoked but to question the girl herself. 'My father was Norse and my great-grandmother came from Aberdeen.'

He made careful anthropological records for many long years. The *Annals of Eugenics*, for October 1950, publishes his article upon 450 male and 450 female infants measured at birth. Still to be published are his records upon 66 male and 60 female children each measured annually from birth to five years, approximately 160 measurements for each one of the 126 children. These measurements are unique in that they refer to the individual child followed for five years—six periods of measurements. A further series deals with twins and triplets measured annually and followed in certain cases for a period of eighteen years. As a rule measurements of this kind at present available do not refer to the individual child followed annually over a period of years, although it is difficult to determine this point from the publications. It is but fitting that acknowledgement should be made of the valuable assistance he received throughout many years from Miss A. M. Clark who was both a remarkably efficient secretary and a talented technician.

As might be expected from his upbringing he had a great love for the land. He had a small garden but it contained a little of everything, and that little was excellent. His lettuces attained the size of cabbages, and his parsley plants almost rivalled kale. Even in the winter months there was always an old-fashioned posy of flowers in his home. He had a boyish delight in beating his brother, a farmer, with early potatoes, although he would confide to his friends that he did not inform his brother about the precautions he took to protect his plants with sacking against a late frost.

He would talk of his boyhood days on the farm, his friendship with a poacher and the poacher's dog. 'When the three of us met the policeman on the road even the dog used to slink past with its ears down, and what a hypocrite I felt because I was good friends with the policeman, too.'

Although usually reserved and reticent, some have known him indulge in delightful descriptions of the fairy spectacle of the almond blossom billowing upon the banks of the Swan River in Western Australia, write with fascination upon the tragedy of the Hapsburgs and the charm of Vienna some fifty years ago, and describe a quaintly pretty interlude in his vacation work at Freiburg. 'It was the custom for colleagues to make a trip into the Black Forest at the week-end. One Saturday two of us climbed the Feldberg for a view of the Alps. We found the hotel near the top full up—food, but no accommodation—and had to make the best of it in a barn nearby, one side packed with newly mown hay, the other occupied by two friendly old horses. We lay just beyond reach of their noses and I had almost dozed off when suddenly in the quiet gloom, broken by the munching of the horses, a soft light swung to and fro as an old peasant entered with his hurricane lamp, set it upon the floor, saw that his horses were comfortable, knelt and told his Rosary, then patting his beasts a final goodnight, left with his lamp a-swinging shadows, while the horses munched beside us in the darkness.'

Serious grey eyes with a pleasant twinkle, set in handsome and distinguished features; an earnest purpose; a gentle unassuming personality; a word that could be depended upon to stand the test of time; courtesy to all people and a kindness to his

pupils in sickness or difficulty that invariably took practical form with visits to hospital and gifts of fruit and sweets left unobtrusively at his departure; these were qualities that endeared him to generations of students. No wonder he was so affectionately known as 'Daddy Low'. No wonder that these students presented him upon his retirement with his portrait etching by Malcolm Osborne and a cheque for some £500, which has been left for the benefit of medical students.

Surely few scientists more worthily fulfilled Wordsworth's demand of the true savant, that he be also a poet in soul and a religionist in heart.

Surely the students at one of Aberdeen's final-year Medical Dinners summed his character excellently in the phrase 'He will give the devil his due'.

Certainly Aberdeen University will never dip her pennant in grateful salutation to a more loyal and devoted son.

One of a family of ten children, Prof. Low is survived by three brothers and three sisters, to whom our deep sympathy is extended. R.D.L.

IN MEMORIAM

L. R. SHORE, M.C., M.A., M.D. (CANTAB.), M.R.C.P. (LOND.), D.P.H.

Lewis R. Shore was born in Dulwich on 16 February 1889. He was the younger son of Dr T. W. Shore, who was a distinguished biologist and for many years Dean of Bart's Medical School. L. R. Shore was educated at Dulwich College, and from there obtained an exhibition to St John's College, Cambridge, where he began a study of medicine which he continued at St Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1913.

At the outbreak of World War I he was House Surgeon to Sir D'Arcy Power, but because he held a regular commission in the R.A.M.C. he was unable to complete the full period of his post. He went to France almost at once and was wounded in the first Battle of Ypres. He was later sent to Gallipoli, where he was awarded the M.C. for his work during the blizzard there; returning to France he was again wounded, at Paschendael in 1918. This time the wound involved the brain, and only through the skill of Sir Percy Sargent did he survive. This wound left a very serious handicap, as he was thereafter subject to severe headaches and to occasional slight attacks of petit mal.

In 1919 he became a demonstrator of anatomy at St Bartholomew's, regarding this primarily as a training for clinical medicine. He completed his M.B., B.Chir., in that year, and took the M.R.C.P. in 1921. It was in 1921 that he married Christine McCallum, who was to be a most devoted wife to him.

In 1922, owing to the appointment of Dr Alexander Macphail as Inspector of Anatomy, Shore became lecturer, and administrative head of the department at Bart's, and realizing his disabilities decided to make anatomy his career. In 1928 he went as lecturer to Johannesburg, but remained there for no more than two years because his headaches were increased by the altitude. Returning to England he went to Cambridge as Demonstrator for a short time, after which he was elected to the Chair in the University of Hong Kong.

He remained in this post until the capture of Hong Kong by the Japanese at the end of 1941. He and his wife were interned in Stanley prison, and there is little doubt that it was only owing to her loving and skilful care that he survived the rigours of prison life until their release in August 1945. But the hardships he had undergone left him a very sick man, and it was some time before he could be evacuated to New Zealand. Indeed he remained an invalid until his death at Rotonia, New Zealand, on 9 February 1950. His ashes are in Lewannick Church, Launceston, beside those of his parents.

He published papers dealing with the distribution of the coronary arteries and the lymphatic drainage of the heart, but his principal researches were concerned with the vertebral column. Five papers on this subject appeared in the *Journal of Anatomy* between 1930 and 1933, and an earlier one, on Spondylolisthesis, was published in the *British Journal of Surgery* in 1928. Writing and the modern concept of research

did not come easily to him, but he excelled in the dissecting room, where he could demonstrate and guide with great care. He disliked mutilating dissection which destroyed the relationship of the parts, and in his teaching constantly reminded his students of the clinical aspects of their studies. He was an excellent colleague, and enjoyed the social side of scientific meetings to the full. He was keen on golf and indeed took an interest in all sports. B.H.

REVIEWS

Entwicklungsgeschichte des Menschen. Ein Grundriss. By KURT GOERTTLER. Gebunden, D.M. 24. Berlin: Springer Verlag. 1950.

In the 271 text pages of this volume Prof. Goerttler has wandered widely from the subject-matter of the title. Indeed only some 50 pages are devoted to human and mammalian embryology and in the remaining, and much longer, part of the book there are numerous excursions into phylogeny, philosophy, metaphysics and even sociology. The result is a presentation which embryologists and general biologists will often find interesting, but it cannot be considered a satisfactory approach for a student. The generalizations often come before, and sometimes without, the description of the relevant facts; and too much is taken for granted in the reader's knowledge.

There is an introductory section dealing with the history of embryological concepts. The survey ranges from Heraclitus to Malthus and Darwin. References are given to Radl and Nordenskiold, but there is no mention of the much more reliable historical works of Needham, Meyer and Adelmann. Indeed, neglect of the non-German literature is a feature of the whole work. Following the historical introduction is a section on the phylogenetic development of animals and on evolution in general. Much of this discussion verges on the metaphysical and can hardly be considered an adequate survey of the problems considered.

The next section of the book is the longest and much the most satisfactory. It deals with the development of vertebrates and with the established laws of their early morphogenesis, and is based largely on the early development of the amphibian and avian egg. As is to be expected in a volume dedicated to Walter Vogt's memory and written by one who has contributed so much in this field, the descriptions of the early embryonic morphogenetic movements and of gastrulation are authoritative. They are accompanied by numerous and informative coloured illustrations based on vitally stained material. Any embryologist will find this part of Prof. Goerttler's volume most interesting though there will not be universal acceptance of all the conclusions.

The last section of the volume deals with some aspects of mammalian and human development and with implantation, placentation and the changes in the maternal organism during pregnancy. It is too brief a consideration of these phenomena to be adequate for students, and the approach is not critical enough for the specialist. There are, too, wide gaps in the presentation, e.g. a complete neglect of the fundamental studies on early human development by Drs Hertig and Rock. The cavalier manner in which human development is treated in a volume purporting to treat of the developmental history of man is unfortunate. But this criticism should not put off the serious embryologist who will find much in Prof. Goerttler's volume to stimulate thought.

J. D. BOYD

Das menschliche Knochenmark, seine Anatomie, Physiologie und Pathologie nach Ergebnissen der intravitalen Markpunktion. By KARL ROHR. (Pp. 404, with 143 illustrations, many in colour; D.M. 47.50). Stuttgart: Georg Thieme Verlag. 1949.

This is the second edition of a monograph on human bone marrow as studied by Arinkin's method of sternal puncture. Written by one of Naegeli's pupils, it bears the stamp of Naegeli's teaching in many respects, even though it departs from it in others. The book is divided into General and Special Sections (Allgemeiner Teil, Spezieller Teil). It is the general section (pp. 1–171) which will be of most interest to anatomists. The coloured illustrations are based on paintings, and on the whole stand out quite clearly; the photomicrographs in black and white are not so satisfactory, and have either been over-exposed in the original photograph, or else over-printed in the reproduction, so that nuclear detail, of such vital importance in the differentiation of marrow cells, tends to become obscured.

Rohr is very conscious of one of the basic defects of the sternal puncture technique, namely that it does not permit of a quantitative study of marrow cells, but merely provides a mixture of marrow and blood in varying proportions. He follows Naegeli—so for that matter do most clinical haematologists—in his attitude toward the lymphocyte population of bone marrow. Though Rohr's own myelogram (adult) gives lymphocytes as 11 % of the nucleated cells of bone marrow, and though he recognizes that in childhood 25 % is an average figure, i.e. one cell out of every four, he nevertheless asserts that the lymphocytes are not part of the marrow parenchyma proper. He backs up this statement with the suggestion that marrow lymphocytes may be derived to a considerable extent from blood admixture, even though his own figures for lymphocyte percentage, taken together with the few data which he cites on absolute marrow counts, show that this explanation is quite untenable.

Rohr effects a radical departure from Naegeli in that he holds the myeloblast to be a relatively unimportant cell in normal marrow, though in pathological marrows the position may be otherwise. Myeloblasts in normal marrow are few and far between, and hence Rohr postulates rather a homoplastic formation of granulocytes from promyelocytes, erythrocytes from proerythroblasts, and so on. In other words, he is a polyphyletist.

However, on occasion there may be other possible lines of development. Thus in cases of augmented erythropoiesis, there is an increase in the number of large reticulum cells. These are the active stage of the small reticulum cells, which closely resemble small lymphocytes; from which it is difficult to distinguish them. One would therefore expect Rohr to be prepared to consider the possibility of the origin of red cells from lymphocytes. But at this point he accepts the teaching of Naegeli, who in turn had followed Ehrlich's lead, that the lymphocytes were a completely independent cell group. Accordingly, he postulated that 'Isomorphie' and 'Isogenie' are not synonymous, and that cells which morphologically are indistinguishable from lymphocytes are nevertheless not lymphocytes. This, though it may possibly be true, means that the classical morphological approach leaves us powerless to solve the problem of the origin of the blood cells, and the significance of the small lymphocyte. It may be noted in this connection that his small reticulum cell seems to correspond to Sabin's primitive cell, which she also found impossible to distinguish from the small lymphocyte.

Anatomists, histologists, and embryologists will find much to interest them in this book, more especially in its General Section. And even where they disagree, their disagreement will be with one who has diligently studied the marrow at first hand. J. M. YOFFEY

Anatomy for Dental Students. By Mary F. Lucas Keene, D.Sc., M.B., B.S. and J. Whillis, M.D., M.S., F.R.C.S. (Pp. viii + 342; 40*s*.) London: Edward Arnold and Co. 1950.

When two experienced teachers of anatomy such as Prof. Lucas Keene and Prof. Whillis join forces to produce a text-book of this kind, one is not surprised to find that what is done is done with competence and skill. Apart from the inevitable occasional misprint, such as epididymus in bold type on p. 194, or Sabotta in the legend to fig. 124, the book is clearly and concisely written, and in parts shows unusual merit. The sequence of figures 158–164, depicting the dissection of the mouth from the inside, is particularly instructive. Chapter xx, on functional activities involving the mouth, nose and pharynx, sets an example which might well be emulated, on a wider scale, by writers of text-books for medical students. It seems doubtful, however, whether the term 'sphincter' is the correct one to apply to the obstruction of the airway produced by pressing the margins of the tongue against the gums and teeth.

One's chief reaction, on reading this book, however, was to consider the somewhat wider problem of the education of dental students. As the authors point out in their preface, the selection of the anatomical facts needed by a student in dentistry presents considerable difficulty mainly because of the limited time available for anatomical studies. Once one

accepts this time limitation, then inevitably one must endeavour to exclude the maximum amount of detail, and retain only such matter as may be regarded as of importance in the daily work of the dentist. In other words, the teaching of the dental student must become exclusively vocational.

This in fact is the approach to dental education which is most frequently adopted, and while it may not immediately have been reflected in the degree of technical competence which dentists possess, it has had grave repercussions on the general level of dental training. The result has been most evident in Universities, where dental students are seen side by side with medical and science students, and where one may readily observe the stultifying effect upon intellectual curiosity of a rigidly vocational approach. Thus in the present work the mechanism of heredity is discussed in one sentence: 'When a cell divides, bodies called chromosomes become evident in the nucleus, and these contain elements termed genes which are responsible for the transmission of hereditary characters to the new generation produced by the division.' It is quite certain that no text-book for medical or science students would dismiss the question in quite so summary a fashion.

It is perhaps beyond the scope of a review such as this to consider possible solutions to the problem. However, a review does present an excellent opportunity for intellectual stock-taking, and serves to focus attention more sharply than otherwise on a situation which has been gradually developing over a number of years.

J. M. YOFFEY

Human Embryology for Medical Students. By S. R. NAIR. (Pp. xiv+398; 241 illustrations; 24*s*. net.) Bombay: The Popular Book Depot. 1950.

The Director-General of Health Services for the Government of India suggests in a foreword to this book by Dr Nair that the study of Embryology requires more support in India than it has received in the past, and he expresses the hope that Dr Nair's book will prove to be that needed foundation on which the Indian student of Embryology may build.

The author states in his Preface that his object has been to give an account of Human Embryology and that no reference to Comparative Anatomy is attempted, but he does include a few figures of sheep embryos.

The text is only half as long as might be expected since every other page is a diagram. Nevertheless, the book contains many fundamental facts without any frills, for of course one would not expect much theorizing in a book of this size, and perhaps for the elementary student of embryology this is just as well.

The book is well printed in a clear type. It contains quite an extensive list of text-books and original papers and if, as may be the case, the study of Embryology has been neglected in India, here is a book that will open up a field full of treasures for the new student.

C. M. WEST

Histology. By ARTHUR WORTH HAM, M.B. (Pp. xix+756; 445 figs.; 10 in. × 17 in.; 80*s*. net.) Philadelphia, London, Montreal: J. B. Lippincott Company. 1950.

This formidable volume is certainly a new and unique presentation of the subject, and asks for a lengthier review than might normally be given to a text-book on Histology written along customary lines.

The book has many unusual features. First of all, it is written in a lively, fluent style. Metaphors and similes abound in it, and some of them are strikingly conceived and carried through with unfailing logic and consequence. Large parts of the book read like a fine story which keeps the attention of the reader and holds his interest.

Secondly, it places Histology in a key position, relating it continuously to other subjects such as gross Anatomy, Physiology, Biochemistry, Pathology and Medicine; and on frequent occasions not only are these links stressed but extensive excursions are made into these branches; for instance, into bone pathology, skin burns and grafting, cancer and clinical endocrinology, in which fields the author draws from his own research experiences.

These digressions, though occasionally somewhat masking the central subject, again add much to the liveliness of the presentation and should make the student aware of the wider background against which the study of normal histological sections has to be seen.

Thirdly, there is the didactic, pedagogic outlook which pervades the text. For, apart from being a text-book of Histology, it will and does—at least in many parts—serve as a practical guide as to how to see things in a section, how to recognize, how to diagnose. The problem of three-dimensional visualization—a stumbling-block for many students—together with common artifacts is given a special chapter illustrated with large-scale drawings and photomicrographs. Almost every conceivable confusion which might be aroused in a student's mind during the course of histological study is dealt with. In fact, all the instructions, warnings, hints, etc., which every experienced teacher of the subject will give to his students orally in the course of class work (i.e. study of sections), are here put into print. This makes the book unique in itself and invaluable for anyone who embarks on teaching this subject. Most valuable, too, is the great number of leading references at the end of each chapter.

With so much of the balance of the text shifted to pedagogic, physiological and clinical considerations, it is only natural that some of the actual histological description of tissues and organs will show some shortcomings and here and there lack in accuracy, precision and completeness. The reviewer may be allowed to point to a few: No distinction is made between plasmosomes and karyosomes; to take the hepatic cells as an example for showing the lack of cell boundaries seems to the reviewer an unhappy choice. Reticular and elastic fibres have not received the precise description they deserve; and the account of the cellular content of loose connective tissue is rather incomplete. Little is said about the appearance of erythrocytes in a fresh drop of blood. A description of the histological structure of lymph vessels does not seem to be given anywhere. Whilst the general account of blood vessels, and especially the means of their nutrition, is exceedingly good, the vascular apparatus of individual organs has sometimes—as for instance in the case of the pulmonary arteries and veins—received little or no attention. The intestinal villus is badly illustrated, and the fine channels passing through the striated border of the intestinal epithelium, so beautifully demonstrated by Baker's work (*Quart. J. micr. Sci.* **84**, 73 (1944)) and which, together with the surrounding cytoplasm, actually account for the striations, are not referred to.

The author indicates in his preface that, in accordance with the modern trend of allocating the teaching of the C.N.S. and its microscopic structure to the neuro-anatomist, only a general description of this tissue is included. Nevertheless, one would have expected in a book of this kind some more exact details, with suitable illustrations, of the elements of nervous tissue than are actually given. The structure of autonomic ganglia is not described at all, yet a lengthy and very good chapter is devoted to the Anatomy and Physiology of the Autonomic Nervous System with reference to emotions and psychosomatic conditions.

However, such deficiencies and shortcomings are outweighed by highlights of accurate and vivid descriptions in most parts of the book. It is impossible to comment on all of these, but some deserve special mention. There is a most lucid chapter, beautifully illustrated, on tissue fluid and the various mechanisms involved in the formation of oedema. The chapter on bone is one of the most exciting and most original. It shows the didactic approach especially clearly and gives a unique exposition, accompanied by most instructive drawings (figs. 135, 136) of the formation of Haversian systems. There is a masterly account, well illustrated, of the tooth and its development; a most careful description of the pancreas, in which the student's eye is literally guided over the slowly moving slide under the microscope. The islets of Langerhans (dealt with at length appropriately amongst the endocrine organs) are equally lucidly described together with their functional aspects.

The author also succeeds well in steering clear of the dangerous reef of haemopoiesis. His description of blood cell development, especially of that of erythrocytes, is concise and clear and avoids unnecessary confusion, even if one cannot subscribe to all the views expressed. The presentation of the haemopoietic tissues in general, however, leaves something to be desired. There is no proper description of a bone marrow section; apart from two general diagrams no further illustrations are devoted to lymph nodes; and it is questionable whether

the student can profitably study the structure of the spleen before having become familiar with that of blood vessels. Splenic sinusoids and venous sinuses are not clearly distinguished.

Frequent and adequate references are made to histo- and cyto-chemical aspects of the subject.

The book is profusely illustrated, partly by line drawings, but to a larger extent by photomicrographs, some of which are unfortunately not very satisfactory. The majority of figures are well chosen and most of them are provided with leader-lines and direct annotations; an oversight seems to have occurred in Fig. 228 where the stratum granulosum, the 'Landmark' of the epidermis, has not been annotated.

The author is to be congratulated on an impressive piece of work. Not only has an enormous effort gone into the writing of this book, but love of the subject and profound enthusiasm in teaching it. The book doubtless ranks amongst the foremost text-books of the subject, in fact through its scope and wide range it fills a vacant place among them. It is to be regretted that its high price will, at least in this country, debar it from becoming a general students' text. But no teacher of the subject should be without it.

F. JACOBY

The Life of Vertebrates. By J. Z. YOUNG, M.A., F.R.S. (Pp. xv+767; 497 figures; $9\frac{1}{4}$ in. × 6 in.; 42*s.* net.) London: Oxford University Press, Geoffrey Cumberlege. 1950.

Two of the noticeable features of this book are the high quality of production and the very moderate price. For these our thanks are due to the Oxford University Press. For the rest, the book is a stimulating contribution to our knowledge of vertebrates for which all who are interested in natural history will be grateful to Prof. Young.

The book is not at all a comparative anatomy of vertebrates, it is what it announces itself to be—a life of vertebrates. The format is very pleasing: each page carries its chapter and section number, and the section title as page heading. The Contents are well set out and really are useful, and there is a good index. All this makes reference from one part of the book to another very simple, and is particularly useful when referring to the Bibliography, which is also arranged under chapters.

One of the most delightful features of the book is the illustrations, and Miss Turlington is to be congratulated on the way in which she has made the vertebrates live. As the author says, drawings have been made from life where possible, but in many cases have been copied from photographs. In all cases the results are clear, crisp and lively drawings, no matter how simple they may be; for example, the goose stepping out of p. 423, or the stress reaction of the chamaeleon who is having his tail trodden on and resenting it with a baneful eye (fig. 234).

Prof. Young says in his interesting Preface that the value of the book rests on its stimulating the reader to make his own observations. Whether many of us nowadays have the time or opportunity to study the life of vertebrates is, I fear, doubtful, but the illustrations will, I hope, stimulate those not so inclined towards 'Fieldwork' at any rate to read the books from which some of the illustrations have been copied. He says how much he has enjoyed making the book, and that I can well believe, and it is a pleasure that I am sure will be shared by many readers. He rightly explains early in the book what he means by the life of a vertebrate and says 'when making any observations, whether by dissection or with the microscope, with a test-tube, oscillograph or respirometer, it is necessary continually to think back to the time when the tissue was active in the living body and to frame the observation so that it shall reveal something significant of that activity', a reminder profitable to all teachers of Anatomy.

The author deals in their usual order with the different Classes of Vertebrates, and to give those who have not seen the book some idea of the sort of arrangement, I might give some of the section headings in the two chapters on reptiles, which together cover about 60 pages: 'Chapter XIV. Life on Land. The Reptiles. 1. Classification; 2. Reptilia; 3. The

lizard; 4. Skin and colour of reptiles; 5. Posture, locomotion and skeleton; 6. Feeding and digestion; 7. Respiration, circulation and excretion; 8. Reproduction of reptiles; 9. Nervous system and behaviour of reptiles. Chapter xv. Evolution of the Reptiles. 1. The earliest reptile populations.' The various extinct orders of reptiles are dealt with and the chapter ends with section '21. Conclusions from study of evolution of the reptiles.' The same sort of plan is used for each of the other classes. Prof. Young explains in his Preface that mammalian organization requires more detailed treatment than that of other groups, and that as such treatment would make a single volume too long he proposes to deal with mammalian structure, function and development together with a survey of comparative embryology in another volume. Many will look forward with pleasure to its appearance.

There are many interesting bits of information that one would like to make a note of, but one or two must suffice: What he calls the biomass of some of the vertebrates is fantastic in its magnitude. There are certain African birds whose colour washes out in the rain. There is a very striking map of the migration high road of birds. The chamaeleon's tongue is everted by filling with blood. One would like to know the evidence on which this last statement is based. The printing and general production are very good indeed, and misprints are very few. In short, the book is an outstanding achievement on which Prof. Young is to be congratulated. C. M. WEST

On the influence of Mechanical and Physiological Rest in the Treatment of Accidents and Surgical Diseases, and the Diagnostic Value of Pain. By JOHN HILTON, F.R.S., F.R.C.S. Sixth edition. Edited by E. W. Walls and E. E. Philipp, in collaboration with H. J. B. Atkins. (Pp. xxxiv + 503, 115 illustrations. Price 25*s*.) London: G. Bell and Sons, Ltd. 1950.

Hilton's *Rest and Pain*—that surgical-anatomical classic reflecting glory on Guy's Hospital and the Royal College of Surgeons of the 1860's—has been out of print for too many years since the last issue of the fifth edition in 1930. All those who agree with Prof. Wood Jones that these *Lectures* 'should be read by every medical student once at least during his study of Anatomy, once again during his practical work in the wards, and afterwards as often as possible during his career as a medical practitioner' owe a debt of gratitude to Prof. E. W. Walls and his collaborators for the production of a sixth edition with several new attractive features.

The biographical Introduction by Mr H. J. B. Atkins—with a frontispiece of John Hilton and a Plate of Joseph Towne's wax model of one of his dissections—is most welcome. The increasingly copious footnotes with which Jacobson embellished the four editions for which he was responsible have been replaced by a much less obtrusive series of simple explanatory notes where some elucidation of terminological and other points seemed necessary for the sake of the student of to-day. General comment on Hilton's anatomical and physiological outlook has been very suitably concentrated in a series of brief editorial Appendices to each of the original Lectures. These Appendices—seventy-two in number and illustrated by seven additional figures—stating succinctly recent advances on numerous lines, provide a valuable commentary on this classical work and frequently show how original Hilton was in his anticipation of the essence of modern views.

This edition, completed by biographical and general indices, is produced in excellent style; and it is certainly worthy of the fame of Hilton's *Rest and Pain*. J. C. BRASH

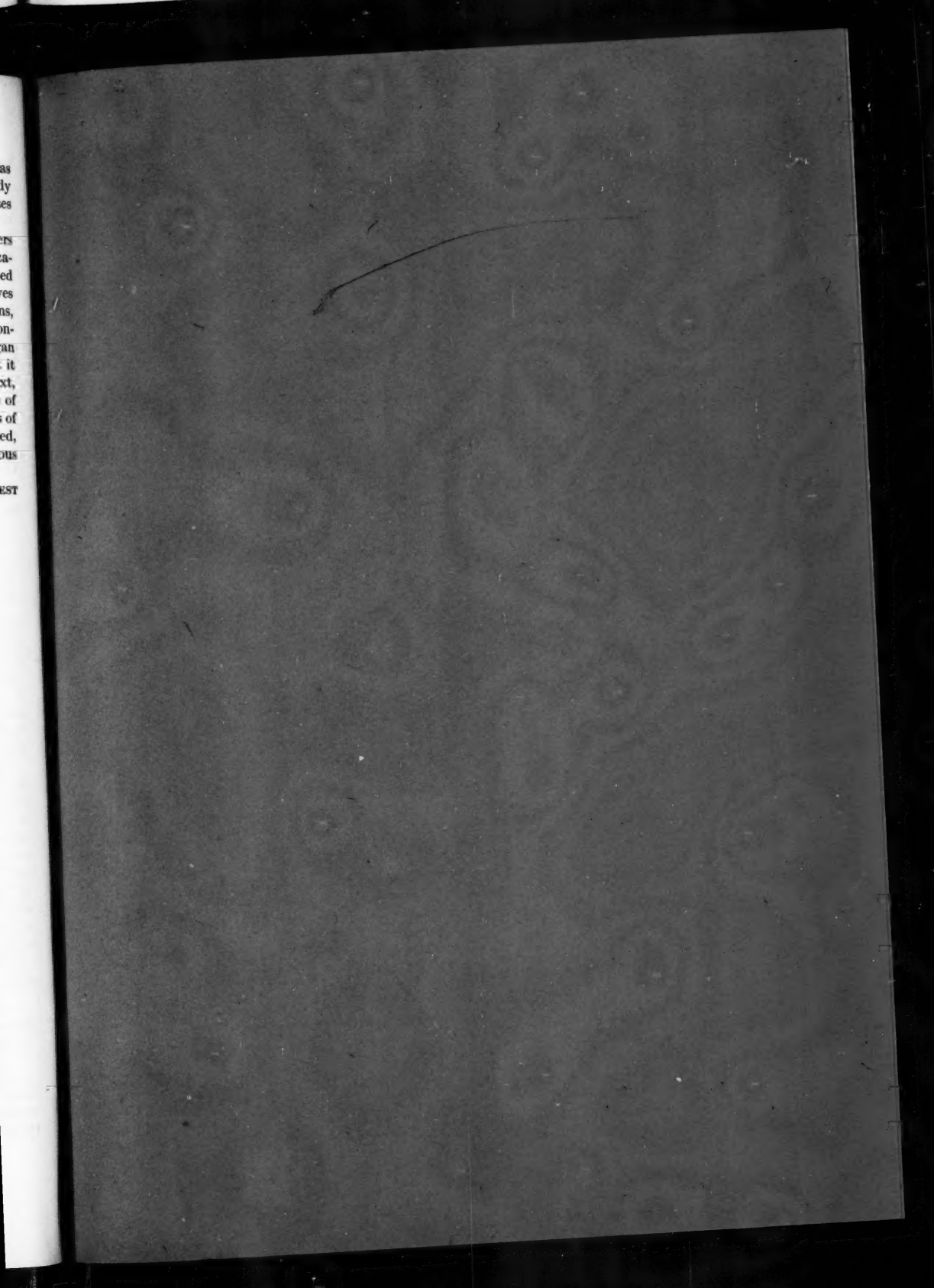
Functional Anatomy of the Vertebrates. By DANIEL P. QUIRING, Ph.D. (Pp. xi + 624; 257 figures; 9 in. × 6 in.; 47*s*. net.) New York and London: McGraw-Hill Book Company Inc. 1950.

In an unusual Preface in which he suggests that, with a 'Faustian outlook', the 'small voice of reflection may be stilled' and the 'weight of the past may be undervalued' the author pays tribute to the pioneers in biology of the past two centuries, and acknowledges the founda-

tions built by them on which his own book largely rests. Nevertheless, as he states, and as is evident from many of the photographs, the book is also based on his own personal study in the field and in the laboratory. He also says, and the title implies, that the book 'stresses function more than is usual in text-books of comparative anatomy'.

The last of the fourteen chapters in his book is entitled 'Functional Anatomy'. It covers 11 of the 527 pages of text, and is concerned mainly with what the author calls the cephalization, thyroidization, adrenalization and heart development in the vertebrates all expressed in graphs. Numbers seem to have a great fascination for the author. He frequently gives the weight of the carcasses of animals he has studied, elephants, sea-cows, cetaceans, buffaloes, and the weights of their testes or lengths of intestine, or weights of stomach contents, and the book ends with an appendix in which there are given the body and organ weights of 3581 vertebrates. This might be very useful information at some time, but it does not really explain the function of the organs. The book is a comparative anatomy text, with rather more photographs than is usual, but very little more about function. Some of the chapters end with what the author calls a 'Sidelight'. These give interesting accounts of his experiences in the field in Africa. Some of the photographs hardly show what is intended, and some of the figures are very poor. Misprints are very numerous, some of them so serious as to lead students astray. There is a glossary that is not very informative.

C. M. WEST



CONTENTS OF PART 3

PAGE

K. J. HILL. The glands of the mucous membrane of the goat abomasum (with Plates 1 and 2 and 2 Text-figures) 215

J. JOSEPH. Further studies of the metacarpo-phalangeal and interphalangeal joints of the thumb (with Plate 1 and 4 Text-figures) 221

J. JOSEPH. The sesamoid bones of the hand and the time of fusion of the epiphyses of the thumb (with 2 Text-figures) 230

G. WEDDELL and E. ZANDER. The fragility of non-myelinated nerve terminals (with Plates 1 and 2) 242

R. WHEELER HAINES. The extensor apparatus of the finger (with 8 Text-figures) . . 251

A. PEACOCK. Observations on the pre-natal development of the intervertebral disc in man (with Plates 1–4 and 4 Text-figures) 260

J. A. ARMSTRONG. An experimental study of the visual pathways in a snake (*Natrix natrix*) (with Plates 1–3 and 2 Text-figures) 275

R. WARWICK. Anatomical note: A juvenile skull exhibiting duplication of the optic canals and subdivision of the superior orbital fissure (with Plate 1) 289

IN MEMORIAM: G. D. Channell 292
Alexander Low 293
Professor L. R. Shore 296

Reviews 298

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